DISSERTATION

on

CORRELATION OF SERUM AMYLASE, LIPASE AND CREATINE KINASE IN PREDICTING THE SEVERITY OF ORGANOPHOSPHORUS POISONING

Submitted in partial fulfilment of requirements for

M.D. DEGREE BRANCH I

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CERTIFICATE

This is to certify that this dissertation entitled **"CORRELATION OF SERUM AMYLASE, LIPASE AND CREATINE KINASE IN PREDICTING THE SEVERITY OF ORGANOPHOSPHORUS POISONING"** submitted by **Dr.M.SHIVANATHAN** appearing for M.D. Branch I - General Medicine Degree examination in MAY-2019 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfilment of regulations of the TamilNadu Dr. M.G.R. Medical University, Chennai. I forward this to the TamilNadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

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DECLARATION

I solemnly declare that the dissertation titled **"CORRELATION OF SERUM AMYLASE, LIPASE AND CREATINE KINASE IN PREDICTING THE SEVERITY OF ORGANOPHOSPHORUS POISONING "** is done by me at Madras Medical College & Rajiv Gandhi Govt. General Hospital, Chennai during 2018 under the guidance and supervision of Prof.Dr.R.PENCHALAIAH., M.D, Prof.Dr.K.S.CHENTHIL., M.D. and Prof.Dr.S.RAGUNANATHANAN., M.D. The dissertation is submitted to TheTamilnaduDr.M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

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ABBREVIATIONS

OPC	-	Organophosphate compounds
Ach	-	Acetylcholine
Ch	-	Choline
S.AchE	-	Serum Acetylcholinesterase
S.Amy	-	Serum Amylase
S.Lipa	-	Serum Lipase
S.CK	-	Serum Creatine Kinase
BchE	-	Butryl cholinesterase
POP	-	PeradeniyaOrganophosphorus Poisoning
U/L	-	Units per Litre
CNS	-	Central nervous system
EChe	-	Erythrocyte Cholinesterase
IMS	-	Intermediate syndrome
P2AM	-	Pralidoxime
OPIDP	-	Organophosphate Induced Delayed Polyneuropathy
COPIND	-	Chronic Organophosphate Induced Neuropsychiatric Disorder

CONTENTS

INTRODUCTION

INTRODUCTION

Agriculture constitutes the major component of Indian economy. Incidence of poisoning by pesticides and consequent admission to the hospital has been increasing in recent decades. OPC ranks the foremost in the list of agents which cause pesticide poisoning. OPC are widely used insecticides in agricultural industry and are common causes of morbidity and mortality due to poisoning worldwide especially in developing countries like India.

Due to easy availability and low cost OP compounds poisoning are becoming a major source of health hazard hence it is important to recognize the entire spectrum of symptoms. Causes of poisoning are suicidal, accidental and homicidal. Suicidal poisoning is the most common cause in developing countries because of its cheapness and easy availability in the market.

The morbidity and mortality depends on the time lag between the exposure and the onset of management. Identification, risk stratification, early diagnosis and prompt treatment of OP poisoning victims are equally vital.

World Health Organization (WHO) estimates that around 0.3 million people die every year globally due to various poisonings and pesticide poisonings causes more than 2,20,000 deaths in developing countries like India because of cheap and easy availability of highly hazardous pesticides. In many Indian reports, the rates of poisoning as suicidal method range from 20.6% (10.3% organophosphorus) to 56.3% (43.8% organophosphorus).

Laboratory evaluation play a crucial role in confirmation and assessing severity of OPC poisoning. Serum acetylcholinesteraselevel is measured in OPC poisoning. It is not specific and does not correlate with the severity of poisoning and cannot be used as a prognostic indicator.

Estimation of serum amylase, lipase and creatine kinase is useful biomarkers in organophosporous poisoning. This study is undertaken to know the efficacy of newer biochemical markers like amylase, lipase and creatine kinase as indicators in assessing the severity of organophosphorus poisoning.

AIMS AND OBJECTIVES

AIM AND OBJECTIVES

AIM OF THE STUDY

- Correlate the Serum Amylase, Lipase and Creatine kinase in predicting the severity of Organophosphorous poisoning.

OBJECTIVES OF THE STUDY

- To estimate the serum levels of amylase, lipase and creatinekinase in acute OPC poisoning and to correlate the same with clinical severity score by PeradeniyaOrganophosphorouspoisoning (POP) scale on admission and measured serially till discharge or death of the patient.
- To correlate the serum levels of Amylase, Lipase and Creatine kinase with complications, intermediate syndrome and need for mechanical ventilation and outcome of the patient.

REVIEW OF LITERATURE

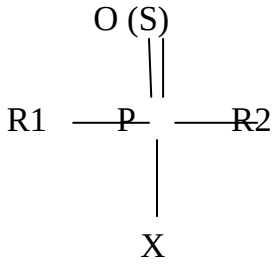
REVIEW OF LITERATURE

HISTORY

OPC are the most commonly used pesticides in agriculture. They have been first synthesized by Lassaigne during early 1800s who observed the alcohol reaction with phosphoric acid. The synthesis of a highly potent compound Tetra Ethyl Pyrophosphate(TEPP) by Phillipe de Clerment in 1854 gave him the honour of conceiving the idea of organophosphorous compound.In 1932 Lange and kreuger, discovered the biological activity of OP esters producing a strong cholinergic effect in human beings and succeeded in the synthesis of dimethyl diethyl phosphor fluoridates . In 1936-1937, Gerhard Schrader, German scientist also noticed similar effects. This made Schrader to synthesis around 2000 compounds like parathion, tabun, sarinetc.The German military used it as a chemical warfare agents. In 1941, during World War II, the OPC were reintroduced as Insecticides.It was Davies who introduced oximesin the year 1955 and its effectiveness in OPC poisoning. The word “cholinesterase” was introduced by Stedman and his co-workers in 1932. Extensive research lead to find that there are two main type of cholinesterase namely AChE (True ChE) and Pseudocholinesterase.

CHEMICAL STRUCTURE

The structure of OPC compound is



OPC are esters of phosphoric acid in which the central compound is phosphorous atom with a double bond to either oxygen (P=O) or sulfur (P=S) and three side chains, one x group,R1 and R2 may be alkyl, alkoxy, amidomercapten or other groups. X group is the principal metabolite for species identification. The effectiveness as insecticides and the lack of persistence in the environment made the OPC a great popularity. Due to their unstable structure these compounds disintegrate into harmless radicals within days of application. The OPC are used as insecticides in agriculture. Some compounds are used as lubricants, plasticizers and flame retardens. Usage of some of these compounds as very potent agents of warfare is of global significance.

Anatomy and Physiology of Autonomic Nervous System

The autonomic nervous system controls the visceral function of the body.Autonomic nervous system centers are located in the hypothalamus,brainstem and spinalcord. Anatomicaly this system is divided into sympathetic and parasympathetic system. Under sympathetic nervous

system preganglionic fibers exits from spinal cord between first thoracic and second lumbar segments. A parasympathetic fiber leaves CNS through cranial nerves III, VII, IX, X and second to fourth sacral spinal nerves.

Acetylcholine (Ach) is a neurotransmitter found throughout the central nervous system, the sympathetic and parasympathetic autonomic ganglia, postganglionic parasympathetic nervous system, most sympathetic glands and at the skeletal musclemotor endplate.

Ach is first synthesized by BAYER in 1867. The Ach is synthesized in the motor nerve terminal from choline and co-enzyme A (CoA) by a process facilitated by the enzyme choline acetyl transferase.

Choline+Acetyl-CoA $\longrightarrow$ Acetycholine

(Choline Acetyl Transferase)

Acetylcholine: 20% of Ach is Present as free Ach in axoplasm and 80% is contained within the vesicles.

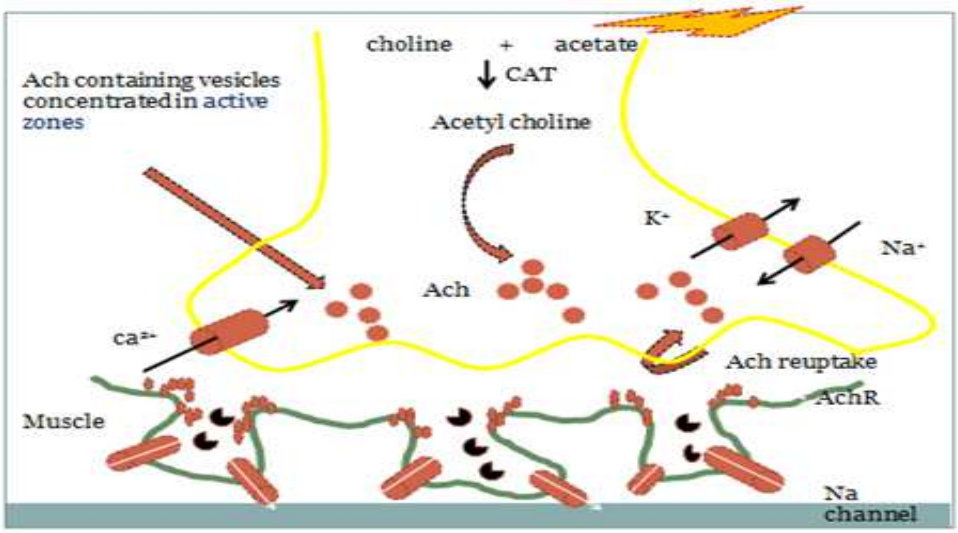
When a nerve impulse arrives at the nerve terminal causing release of acetylcholine into the synaptic space. Ach binds to and activates muscarinic and nicotinic receptors. Duration of Ach is curtailed as it is hydrolysed by the enzyme acetylcholinesterase.

Acetyl choline $\longrightarrow$ Acetate ion + choline

(AChE)

The choline is reabsorbed actively into the neural terminal and reused in forming new acetylcholine. These events takes less than 5-10

milliseconds and within about 20 seconds new vesicles will be formed and within another few seconds acetylcholine is transported into the interior of these vesicles and they are ready for a new cycle of acetylcholinesterase. The actions of acetylcholine in the body depend on the receptors involved and the site.



Activation of the muscarinic receptors stimulates or inhibits cellular function through G protein at visceral smooth muscle, cardiac muscle and secretory glands. Nicotinic receptors are Na channels present in post synaptic membrane and in skeletal muscle motor endplates. The enzyme AchE regulates the activity of acetylcholine within the synaptic cleft.

There are two types of cholinesterase in human body. One is Pseudocholinesterase (PChE) and other is true cholinesterase (True ChE).

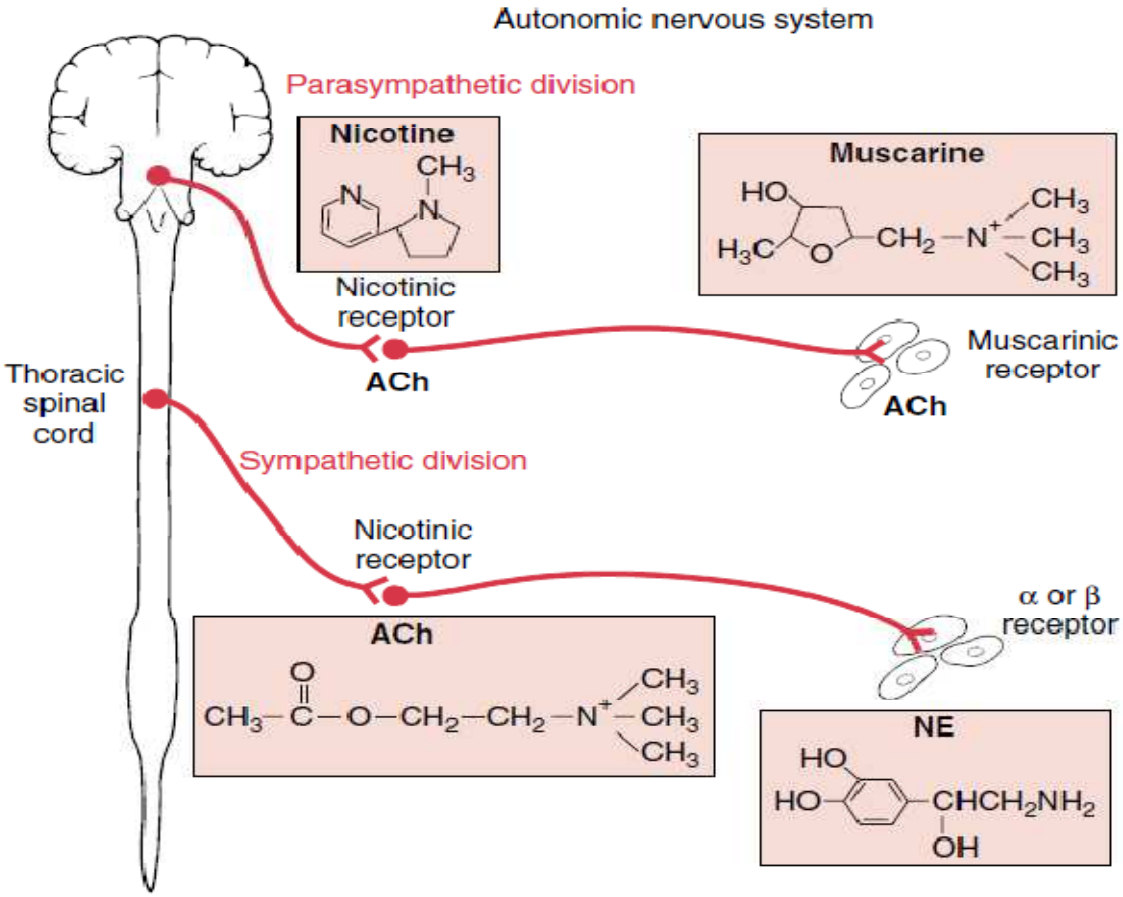
True Cholinesterase- (RBC Cholinesterase)

It is present in erythrocytes, nervous tissue, spleen, lungs and grey matter. It is decreased in pernicious anemia and after antimalarial therapy. Ach is inactivated by combination with two sites on the enzyme RBC cholinesterase anionic site and esteratic site.

Plasma cholinesterase (Pseudocholinesterase)

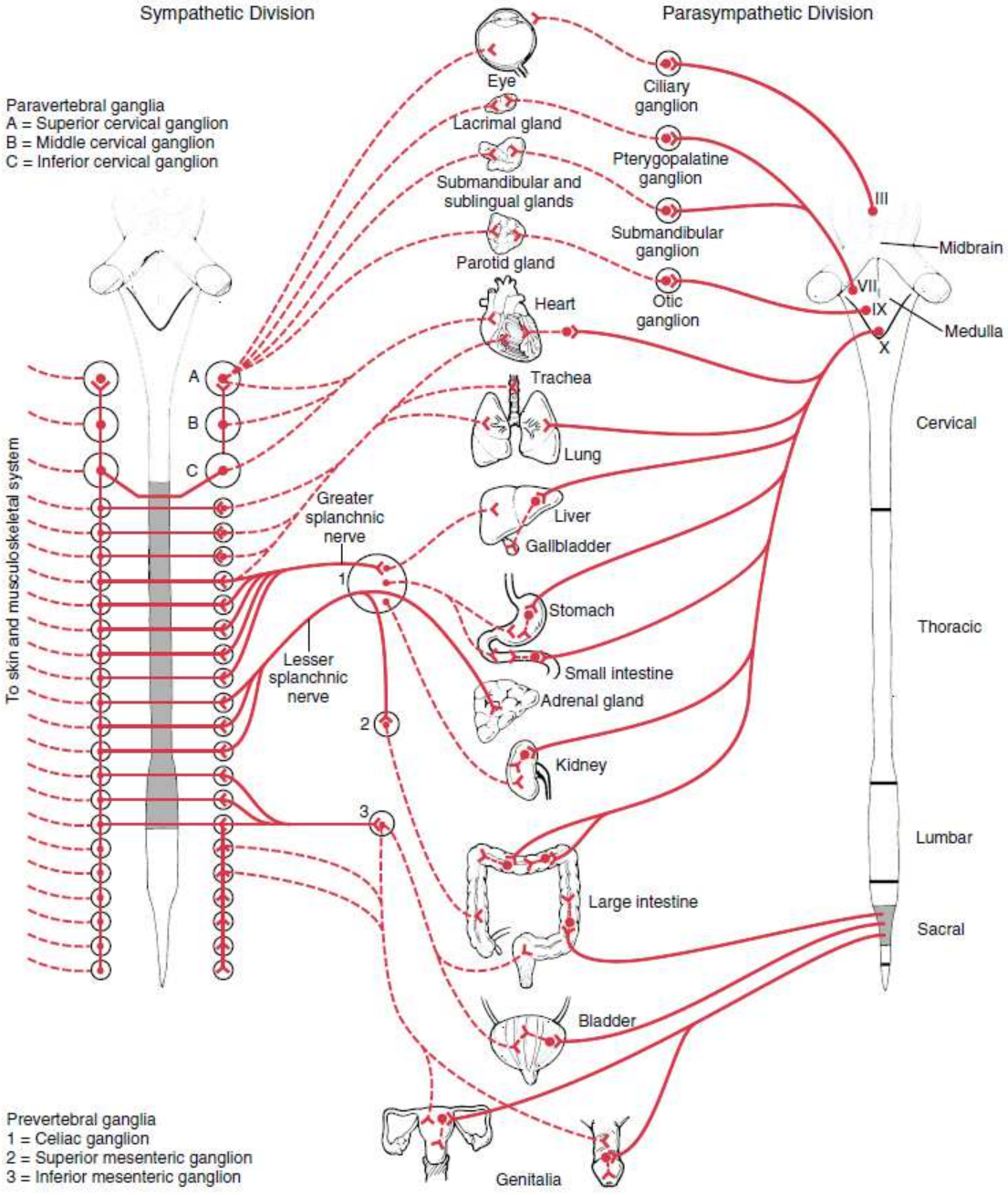
It is found in plasma, pancreas, liver and intestinal mucosa.

NEUROCHEMISTRY OF ANS PATHWAY



THE ORGAN SPECIFIC ARRANGEMENT

OF ANS



Plasma cholinesterase deficiency could be due to physiological variation , disease, iatrogenic causes and genetic defects.

1) Physiological variations:-

a. Age:

- A newborn has about 50% of normal PchE activity.
- PchE activity reaches normal level at puberty.
- In old age (75-80years) the activity is 75% of normal.

b. During pregnancy PchE activity decreases 20 -30%.

2. Diseases

a. Liver disease:PchE activity decreases upto 50% in acute hepatitis, cirrhosis and liver metastasis.

b. Renal disease: PchE activity decreases to 30% normal in renal disease.

3.Drugs: OPC &Organocarbamate compounds, Anticancer drugs,

Ecothiophate eye drops and Bombuteral.

4. Genetic :Patients with atypical PchE have low PchE activity.

CLASSIFICATION OF OPC

I) BASED ON GROUPS

PHOSPHORYLCHOLINES	FLOUROPHOSPHATES	CYANOPHOSPHATES &HALOPHOSPHATES	MULTIPLE CONSTITUENTS
Echothiopate	Dimefox Sarin Mipafox	Tabun	Dimethoxy Diethoxy Dialkoxy Diamino Trithioalkyl Triphenyl Chlorinated Mixed substituent

II) BASED ON CHEMICAL STRUCTURE

A) Alkyl phosphates:

1. HETP (Hexaethyl tetra phosphate)
2. TEPP (tetraethyl pyrophosphate) tetron,fosvex

3. OMPA (octamethylpyrophoramide) schardan13

4. Dimefox (bis[dimethyl amino] flurophosphine oxide)

5. Isopestox (bis[isopropylamino] flurophosphine oxide)pestox

6. Malathion(5,[1,2dicarbethoxyethyl]0,o dimethyl dithiophosphate)

7. Sulfoteppa(tetra ethyl 0,dithiopyrophosphate)-dithione Asp-47

8. Systox,demeton(0,0 diethyl 10-2 ethylmercapto ethyl thionophosphate)

9. Dipterex(0,0 dimethyl 2-2-2 trichloro hydroxyl ethyl phosphate-tug orbait

B) Aryl phosphate

1) Paroxon

2) Parathion

3) EPN-o, ethyl-o-p nitropheyyl benzene thionophosphate, EPN 300

4) Methylparathiono, o-dimethyl o-p nitrophenylthiophosphate

III) BASED ON TOXICITY:

A) Highly toxic(<D_{50}<50 mg/kg)

1. Azinophos-methyl
2. Bomyl
3. Carbophenthion
4. Chlorfenvinphos
7. Cyanofenphos
8. Demeton
9. Dialifor
10. Dicrotophos
11.Disulfoton
12.EPN
13.Famphur15
14.Phenamiphos
22.Monocrotophos
23.Parathio-ethyl

15. Fenophosphan
16. Isophenfos
17. Isofluorphate
18. Mephosfolan
19. Methmidophos
20. Methidathion
21. Mevinphos
24. Parathion methyl
25. Phorate
26. Phostolan
27. Phosphomidan
28. Prothoate
29. Sulfotep
30. Tetraethylpyrophosphate (TEPP)

B) Moderate Toxicity (D_{50}=50-1000mg/kg)

1) Acephate
2) Bensulide
3) Chloropyrofos
4) Crotoxyphos
5) Cythioate
6) DEF
7) Deneton-s-methyl
8) Diazinon
9) Dichlorvos
10) Dimethoate
11) Edifenphos
12) Ethion17
13) Ethoprop
14) Fenitrothion
15) Fenthion
16) IPB
17) Leptophos
18) Merphos
19) Naled
20)Phosalone
21) Phosmet
22)Pirimiphos-ethyl
23) Profenofos
24)Propetaamphos
25) Pyrazophos
26) Quinalphos
27) Sulprofos
28) Thiometon 18
29) Triazophos
30)Tribufos
31)Trichlorfon

C) Low Toxicity(D_{50}=>1000mg/kg)

1) Bromophos

2) Etrimfos

3) Iodofenphos

4) Malathion

5) Phoxim

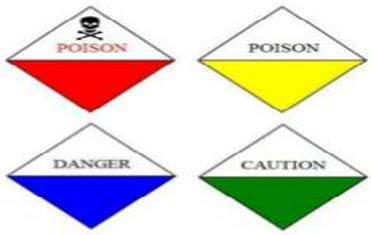
6)Prophylthiopyrophosphate

7) Temephos

8) Tetrachlorrinphos.

Poison :Identification

WHO colour code on container.



Red label	Extremely toxic	Monocrotophos, zinc phosphide, ethyl mercury acetate, and others.
Yellow label	Highly toxic	Endosulfan, carbaryl, quinalphos, and others.
Blue label	Moderately toxic	Malathion, thiram, glyphosate, and others.
Green label	Slightly toxic	Mancozeb, oxyfluorfen, mosquito repellant oils and liquids, and most other household insecticides.

PHARMACOKINETICS OPC is absorbed by ingestion, inhalation, percutaneusly or injection. Most OPCs are lipophilic – adipose tissue accumulation is highest. The pharmacokinetics depends on certain factors such as :

1)Route of administration

2) Distance from target organs

3) Local vs Systemic metabolism and activation

4) Route of elimination

5) Endogenous hydrolysis by non-specific esterase

Metabolism occurs either by hydrolysis by esterases, oxidation or by

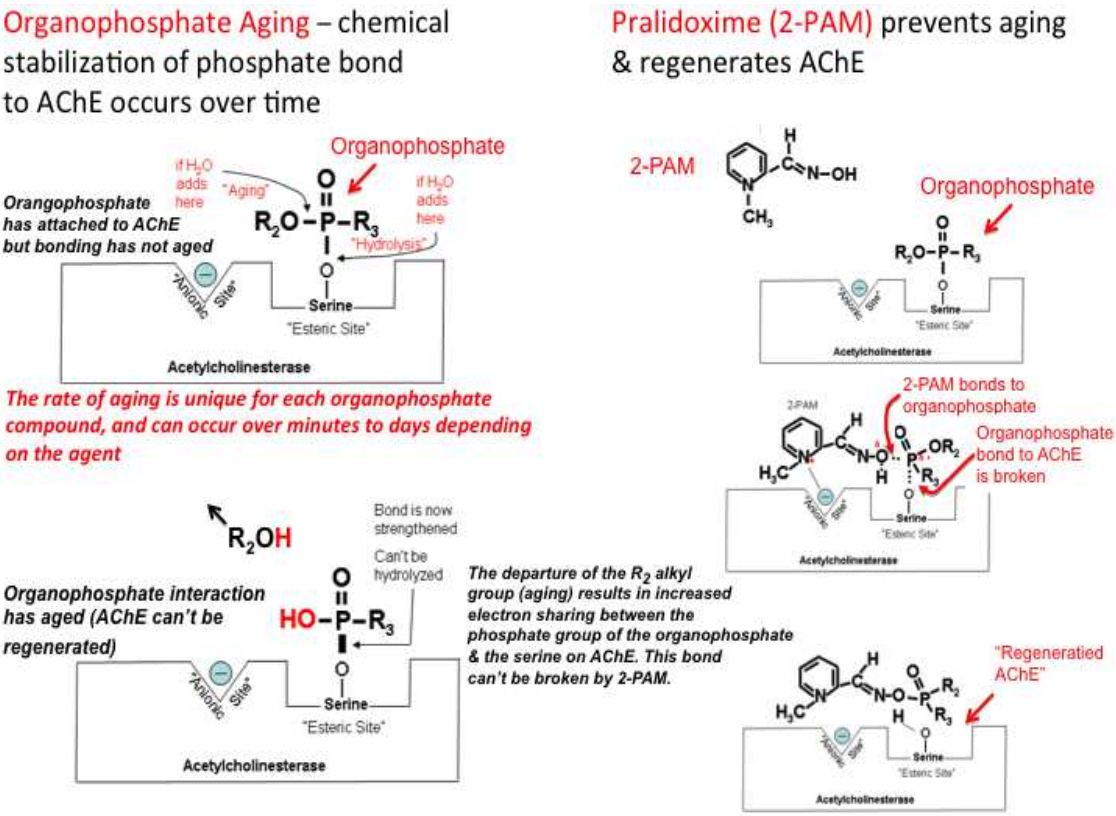
glutathione transfer. Around majority of compound is eliminated within 48 hours of exposure by urinary and fecal excretion.Cholinergic crisis may occur when unmetabolized OPC are mobilized from fat store – Fenthion ,Chlorfenthion.Prolonged absorption from intestine & reabsorption from fat store may allow the insecticide concentration for up to 48 hrs.MECHANISM OF ACTIONOPC inhibit enzyme AChE. The mechanism of inhibition of the enzyme is by reacting with the esteratic site on the acetyl cholinesterase molecule. The bond formed between phosphorus atom and the esteratic site of enzyme is stable and requires hours to weeks to reverse depending on the type of OP compounds. Phosphorylated enzyme is inhibited because of occupation of its active site. It is incapable of carrying out its normal function of hydrolyzing acetylcholine. The effect of the OPC poisoning is therefore the result of continuing increased production of acetylcholine at the neuromuscular junction, resulting in depolarisation block.

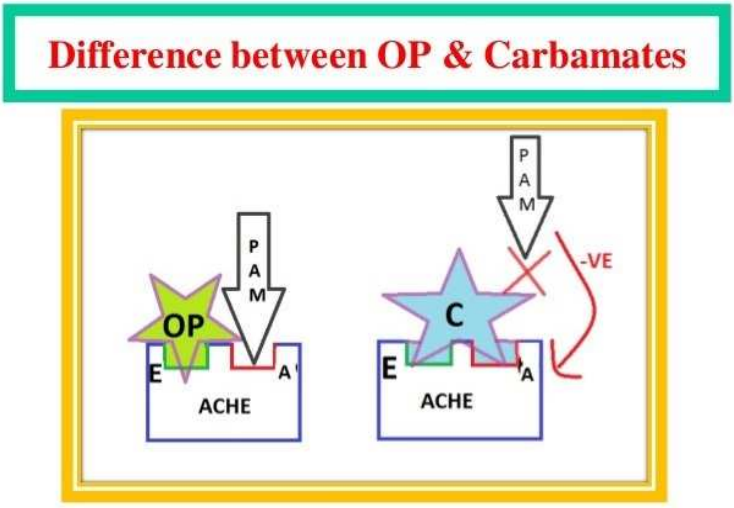
This phosphorylated enzyme can undergo spontaneous hydrolysis or dealkylation. Due to spontaneous hydrolysis active enzyme cholinesterase is released and this is called reactivation. The phosphorylated enzyme can also undergo dealkylation. Once this occurs, reactivation is impossible. This process is called ageing.

AGING OF ENZYME

- OPC -- Ach E - is irreversibly bound for 24 – 72 hours
- When one of the R group leaves the phosphate molecule this step is called aging .
- Denovo synthesis of Ach E is required to replenish the supply once aging has occurred
- Aging can not occur in carbamates.
- Ach E spontaneously hydrolysed in 24 hrs.
- AchE aging is particularly rapid with *dimethyl phosphoryl* compounds such as Malathion, fenthion, metyl parathion, dichlorvos , dicrotophosdicaphon , dimethoate, temephos , crotoxyphos,
- Diethyl OPC low propensity for aging benefit from P2AM.- parathion, chlorpyriphos , phorate , phosfolan, TEPP, coumaphos, diazinon , ehion , chlorothion, demeton.
- Permanent binding to the acetylcholinesterase enzyme (“aging”) may occur after a variable delay unless antidotal treatment with an enzyme reactivator is given.
- Reactivation of inhibited AChE occurs more quickly with dimethylatedOrganophosphatescompared with diethylated OPs.

Antidotal treatment with an oxime may prolong the half-life of aging; early administration of oximes is therefore likely to be valuable.





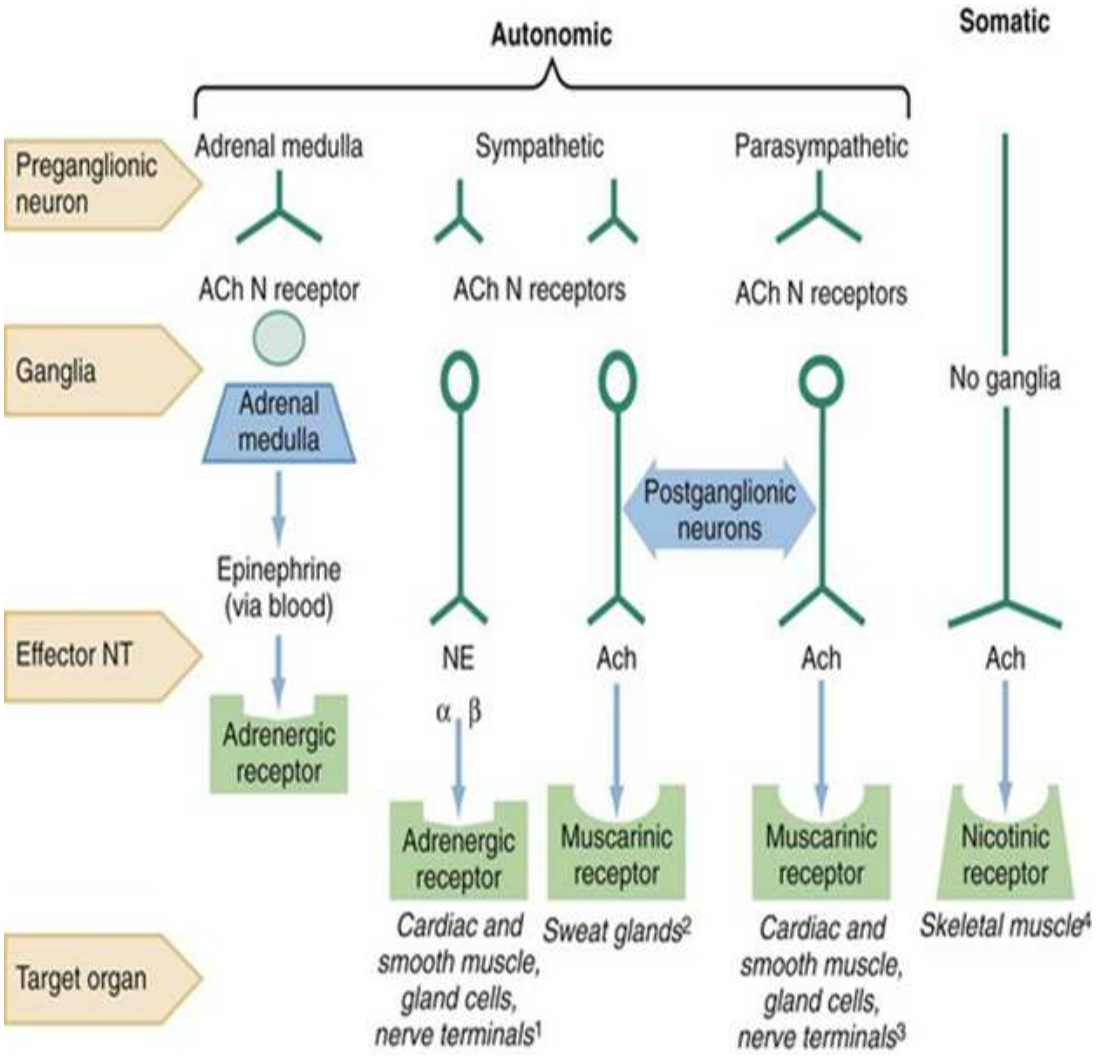
Hence the three independent reactions determine the speed of onset and severity of poisoning i.e.,

1. Phosphorylation of ChE by OPC2. Reactivation 3. Ageing

In acute poisoning clinical manifestations occur after more than 50% of serum cholinesterase is inhibited and severity of manifestations correlates with the degree of inhibition of serum cholinesterase activity.

- Mild poisoning - cholinesterase level reduces to 20-50%
- Moderate poisoning - cholinesterase level reduces to 10-20%
- Severe poisoning - cholinesterase level reduces to lessthan10%.

	Muscarinic receptors (M-receptor)	Nicotinic receptors (N-receptor)
Locations	smooth muscle, gland and cardiac muscle M--- smooth muscle、gland M1--ganglia、gland M2---heart	skeletal muscle-- motor ending-plate (N2 N2), ganglia-postsynaptic membrane(N1),
Effect	inhibiting the cardiac muscle, exciting the smooth muscle & gland	N2:exciting skeletal muscle , N1 exciting the postsynaptic neuron in ganglia
Antagonist	Atropine	N1:hexamethonium N2:decamethonium



CLINICAL FEATURES

The clinical manifestations of OP poisoning depends on the agent, quantity and route of entry. Ingestion and inhalation result in more rapid development of symptoms than dermal exposure. After ingestion symptoms appear within 30-90 minutes and a maximum of 24 hrs in case of compounds which are highly lipophilic and which require metabolic bioactivation.

LOCAL EFFECTS:

GI symptoms appear first before the onset of systemic symptoms. In inhalation typically exhibit respiratory effects. After ocular exposure symptoms generally begins in the eyes.

Systemic effects: Three well defined clinical phases are observed:

1. Initial cholinergic phase.

2. The intermediate syndrome (IMS)

3. Organophosphate Induced Delayed Polyneuropathy.

4. Chronic Organophosphate Induced Neuropsychiatric Disorder

1. The cholinergic phase is mainly due to accumulation of Ach at the cholinergic synapses and may be classified into A) Muscarinic(all postganglionic nerve endings) B) Nicotinic (Autonomic ganglia and skeletal muscle end plate) C)CNS manifestations(synapses in CNS)

A) Muscuranic manifestation:

Gastro intestinal System	Nausea, vomiting, increased salivation, diarrhea, abdominal cramps, tenesmus, fecal incontinence.
Respiratory System	Bronchorrhoea, Rhinorrhea, dyspnoea, wheeze, cough, pulmonary edema, cyanosis.
Sweat glands & Lacrimal glands	Increased sweating & lacrimation

Cardiovascular system	Bradycardia, hypotension and arrythmias.
Genitourinary	Urinary Incontinence
Eyes	Miosis,Diplopia and Lacrimation

B)Nicotinic manifestations:

Striated muscle	Muscle twitching, cramps, fasciculation, respiratory muscle weakness.
Sympathetic ganglia	Pallor,tachycardia, hypertension.

Cholinergic Toxidrome	
Muscarinic Symptoms	**Nicotinic Symptoms**
S – Salivation	**M** – Muscle cramps
L – Lacrimation	**T** – Tachycardia
U – Urination	**W** – Weakness
D – Defecation	**T** – Twitching
G – GI cramping	**F** - Fasciculations
E – Emesis	

C) Central nervous system manifestations:

Anxiety, restlessness, giddiness, emotional liability, slurred speech, ataxia, seizure, drowsiness, confusion, difficulty in concentration, headache, nightmare, insomnia, excessive dreaming, apathy, tremor, depression, generalized weakness, coma, absence of reflexes, cheyne-stokes respiration,

depression of respiratory and circulatory centres with Dyspnea, Hypotension and Cyanosis.

2. The Intermediate Syndrome (IMS)

After apparent recovery from cholinergic crisis muscle paralysis occurs, but before the expected onset of the delayed polyneuropathy has been identified as “Intermediatesyndrome(IMS)”. This is type II paralysis first described by Wadia et al. In 1974 and later christened as “Intermediate syndrome(IMS)” by Senanayake,Karalliedde L. The syndrome is of Acute onset, seen within 24-96 hrs(1-4days) after poisoing, affecting conscious patients without fasciculations or other cholinergic manifestations. The cardinal features of this syndrome is muscle weakness affecting predominantly proximal limb muscles and neck flexors.The muscles innervated by motor cranial nerves III,VII and X are affected in different combinations. These patients were conscious and showed marked anxiety, sweating, dyspnoeic and restlessness caused by progressive hypoxia.

The neck muscle weakness was a constant feature. Patients were unable to raise head above the pillows. Weakness of shoulder abduction and hip flexion was also noted. However normal strength in the distal muscle gives a false impression that the limbs are spared. Tendon reflexes are diminished or in most patients with no sensory impairment. Complete recovery occurs within 4-18 days if adequate ventilator support is given. But altered function at neuromuscular junction may persistupto 2 yrs after its occurrence.

The syndrome carries great mortality if not recognized in time and treated. The agents commonly responsible are fenthion, monochrotophos and Dimethoate. Respiratory insufficiency develops over 6 hrs approximately. Initially patient uses accessory muscles of ventilation. There is increase in ventilator rate, sweating, restlessness and later cyanosis if not recognized patient soon becomes unconscious and death follows. A consensus from literature search appears that IMS may result from inadequate therapy with oximes.

IMS is likely to result from post synaptic neuromuscular dysfunction. The symptom complex begins at a time when the cholinesterase function is very low and the OP compounds is still detectable in the body. As blood levels of OPC's fall and OPC's tissue redistribution occurs the motor end plates may be rechallenged by the cholinesterase inhibitor in the presence of inadequate circulatory oximes.

3. Organophosphate Induced Delayed Polyneuropathy (OPIDP)

Though uncommon in India, it is a distal motor axonopathy develops following a latent period of 2-4 weeks after the cholinergic crisis. The main clinical features are distal muscle weakness especially of feet and hand. The weakness is preceded by limb pain and parasthesia. Wasting of distal muscles of particularly small muscle of the hand and those of anterior and peroneal compartments of the leg is a inevitable consequence. In some patients pyramidal tract signs appear after a few weeks or few months. Recovery is

variable. The phosphorylation of an enzyme neuropathy target esterase in nervous tissue is considered to be responsible for the polyneuropathy. Several out breaks of OPIDP have occurred in various countries where the poison was traced in most instances to be accidental contamination or adulteration of cooking oils with mineral oils. In 1930's more than 50000 US citizens became paralysed after drinking Jamica ginger contaminated with TOCP.

4. Chronic Organophosphate Induced Neuropsychiatric Disorder (COPIND)

These are the delayed complications due to acute exposure to high dose of OPC. The manifestations are depression, anxiety, memory disturbances, dystonic reactions, cog-wheel rigidity, schizophrenia. It is due to the sequelae of convulsions, respiratory failure, cardiacarrythmias and anoxia.

CLINICAL SEVERITY SCORING

The following grading of clinical severity are useful in OPC poisoning :-

1.Modified Dreisbach Clinical Criteria

2. Poisoning severity Scale (PSS)

3.Peradeniya Organophosphorus Poisoning Scale (POP Scale)

Senanayake N.(1993) proposed ParadeniayaOrganophosphorus Poisoning (POP) scale for grading the severity is the commonly used one.

POP SCALE

PARAMETERS	Score 0	Score 1	Score 2
PUPIL SIZE	≥2 mm	<2mm	Pinpoint
RESPIRATORY RATE	<20/min	≥20/min	≥20/min with central cyanosis
HEART RATE	>60/min	41-60/min	<40/min
FASCICULATION	None	Present Generalised/continuous	Both generalised and continuous
LEVEL OF CONSCIOUSNESS	Conscious and rationale	Impaired response to verbal commands	No response to verbal commands
SEIZURE	Absent	Present	-
GRADE (Score)	Mild (0-3)	Moderate (4-7)	Severe (8-11)

The revised grading for Bardin et al (1990) for OPC poisoning severity includes the history of intake exposure to organophosphorus, attempted suicide, clinical signs and makes use of investigations(decreased PaO2 and abnormal chest Xray) in early assessment of respiratory failure.

Revised grading for organophosphoruspoisoning : Grade Criteria

Mild poisoning : History of intake/exposure

Mild signs:

- Normal consciousness
- Secretions 1+
- Fasciculations 1+

Severe poisoning : Severe signs:

- Altered consciousness
- Secretions 3+
- Fasciculations 3+

Life threatening poisoning : Suicide attempt

- Stupor
- PaO2<75mm Hg(<10mm Hg)
- Abnormal chest roentgenogram.

MANAGEMENT

DIAGNOSIS

1. History or evidence of exposure to organophosphate.
2. Signs and symptoms of poisonoing.

3. Improvement of these signs and symptoms after the administration of Pralidoxime and atropine.

4. Inhibition of cholinesterase activity of blood.

Diagnosis is based on the history of exposure and the presence of characteristic muscarinic, nicotinic, and CNS manifestations of acetylcholine excess.There may be a solvent odor, and some agents have a strong garlicky odor.

- Blood/serum chemistry :
  - ✧ Serum electrolytes, Random blood glucose, Serum creatinine
  - ✧ Hematology (including white cells count as leukocytosis is common)
  - ✧ PlasmacholinesteraseSequential rise of plasma cholinesterase activity every few days for 14 to 28 days may confirmation of organophosphate exposure in the absence of pre exposure baseline values.
  - ✧ Serum Amylase
  - ✧ Serum Lipase
- ✧ Serum Creatine Kinase
  - ✧ Serum levels of organophosphorus compounds and their metabolites.

- Arterial Blood Gas :
    - ✧ Arterial blood gas analysis in patients with CNS or respiratory depression.
- Urine analysis :
    - ✧ Estimation of excretory products of organophosphorus agents.
- Chest radiograph : For respiratory failure
- Electrophysiological studies :It is useful in neurological features
    - ✧ Electromyography
    - ✧ Single fibre electromyography
    - ✧ Train of four
- Laryngoscopy : To evaluate vocal cord functions indirect laryngoscopy is useful
- Ultra sound/CT scan :To evaluate pancreatic status
- Positron emission tomography : To estimate cortical visual loss following respiratory failure.

TREATMENT

I) ACUTE CHOLINERGIC CRISIS

All patients should be managed as emergencies in hospital.

A. First aid

B. Prevent further absorption of insecticide

C. Specific antidote therapy

1. Anticholinergic medication

2. Reactivation of Aectylcholine-oximes

D. Benzodiazepines

E. Other medications

Mild poisoning: Warrants admission to hospital for atleast 72 hrs for observation and treatment.

Moderate poisoning: admission in ICU.

Severe poisoning: merit immediate transfer and admission to ICU.

A. First Aid:

a) Remove patient from the contaminated environment.

b) Remove contaminated clothing.

c) Wash skin with soap and water and eyes with water.

d) Assess breathing and circulation.

e) Resusciate if necessary

f) Support vital function if necessary

- O2 inhalation
- Lung ventilation
- Ionotropes

g) Control of convulsion

h) Monitor ECG, blood pressure, O2 saturation,ventilation,level of consciousness.

B. Prevent further absorption of insecticide:

a) Gastric lavage: performed using largest possible oro-gastric tubes with 50-100ml of fluid/lavage, preferably within 1 hr of ingestion protect airway in patients with impaired consciousness.

b) Administer activated charcoal: dose initial 60-100 gms, followed by 0.25 gms to 0.5gms/kg every 1-4 hrs.

C. Specific antidotal therapy: Treatment aims:

a) Reversal of synaptic biochemical abnormalities.

b) Reversal of cholinesterase blockade.

This is activated by administering sufficient quantity of two complimentary medications.

i) Anticholinergic medication- atropine or glycopyrrolate.

ii) Reactivation of AchE-oximes.

i) **Anticholinergic medication:** Atropine:

It is a tertiary amine, a competitive antagonist of acetylcholine at muscuranic post synaptic membrane and in the CNS. In symptomatic poisoned adults

- Inject 1.8-3 mg (3-5 ml) of atropine, bolus. Check whether targets are achieved.
- Aim for heart rate >80 beats per minute, SBP > 80 mm Hg, and a clear chest (atropine won't dry focal areas of aspiration).Double the atropine dose every five minutes if you have not achieved these Targets.
- Review patient every 5 min. Once these parameters start improving. Repeat last same or smaller dose of atropine.
- If improvement in these parameters is persistent and satisfactory after 5 min, now you can plan for atropine infusion.Calculate total dose of atropine required for rapid atropinisation.
- Start hourly atropine infusion at 20% of total dose of atropine required for atropinisation. Most patients do not need >3-5 mg (5-9 ml) per hour of atropine infusion.

- Use Targets checklist to reduce infusion rate by 20% every 4 hourly once your patient is stable
- Do not use oral secretions to guide therapy in patients who are intubated, unconscious, having oropharyngeal airway in situ and with intermediate syndrome.Ignore sweating to adjust atropine dose.
- Stable Patients with clear chest but heart rate just below target do not need further more atropine.
- Bronchorrhoea is the most important sign for titrating dose of atropine once patient is stable.
- Atropine toxicity= absent bowel sounds + fever + confusion.
- Stop atropine infusion for 60 min, if patient has developed atropine toxicity.
- Re-start infusion at 80% of initial rate, once the temperature comes down and the patient gets calm.
- **PRALIDOXIME**

  For whom ?
- Only to treat Organophosphorus poisoned patients.

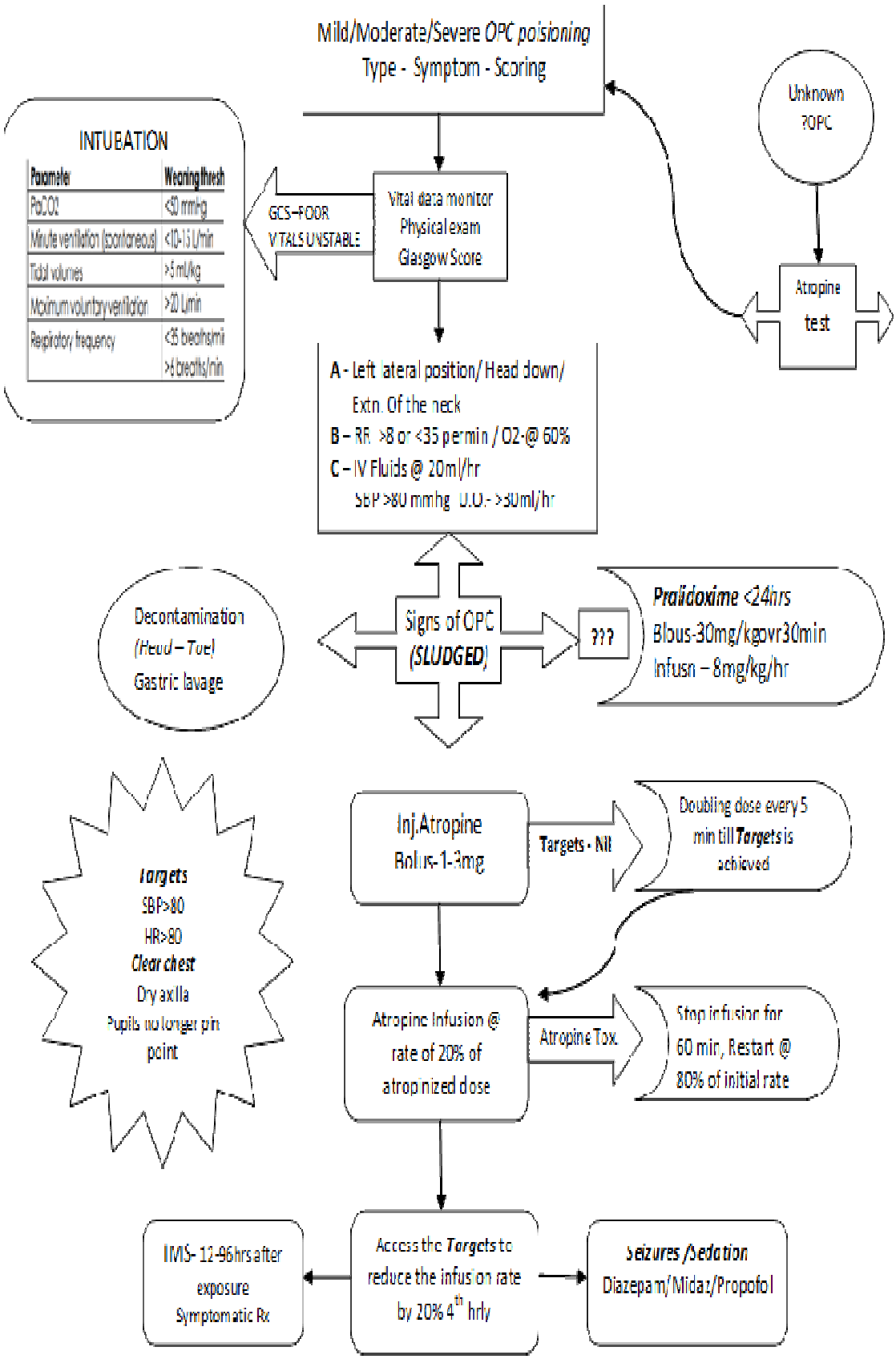
  How much ?
- Bolus dose: 30 mg/kg PAM over 30 minutes. Adults-2g
- Obidoxime @ 4mg/kg over 20 min
- Maintenance dose: continuous infusion of 8 mg/kg per hour. Adults-500mg/hr
- Obidoxime- 0.5mg/kg/hr infusion

How ?

- PAM must be given by Infusion. Go slow, both for bolus and maintenance. A fast infusion can cause vomiting, hypertension, cardiac arrhythmia or a cardiac arrest.
- Effectiveness of pralidoxime differs according to the class of Organophosphorus compounds. In Profenofos P2AM is not effective.

  In dimethyl Organophosphorus compound PAM is effective upto 12 hours. And in diethyl Organophosphorus compound upto 5 days.

- Pralidoxime is not generally recommended for carbamate intoxication, because in such cases the cholinesterase inhibition is spontaneously reversible and short-lived.
- However, if the exact agent is not identified and the patient has significant toxicity, pralidoxime may be be given empirically.


Mild/Moderate/Severe OPC poisoning
Type - Symptom - Scoring
Unknown POPC
Atropine test
INTUBATION
Parameter | Weaning threshold
PaCO2 | <50 mmHg
Minute ventilation (spontaneous) | <10-15 L/min
Tidal volumes | >5 ml/kg
Maximum voluntary ventilation | >20 L/min
Respiratory frequency | <35 breaths/min >4 breaths/min
GCS<8 OR VITALS UNSTABLE
Vital data monitor
Physical exam
Glasgow Score
A - Left lateral position/ Head down/ Extn. Of the neck
B – RR >8 or <35 per min / O2 @ 60%
C – IV Fluids @ 20ml/hr
SBP >80 mmHg U.O. - >30ml/hr
Decontamination
(Head – Toe)
Gastric lavage
Signs of OPC
(SLUDGED)
???
Pralidoxime <24hrs
Bolus-30mg/kg over 30min
Infusn – 8mg/kg/hr
Targets
SBP>80
HR>80
Clear chest
Dry axilla
Pupils no longer pin point
Inj.Atropine
Bolus-1-3mg
Targets - Nil
Doubling dose every 5 min till Targets is achieved
Atropine Infusion @ rate of 20% of atropinized dose
Atropine Tox.
Stop infusion for 60 min, Restart @ 80% of initial rate
Access the Targets to reduce the infusion rate by 20% 4th hrly
IMS- 12-96hrs after exposure
Symptomatic Rx
Seizures /Sedation
Diazepam/Midaz/Propofol

D) BENZODIAZEPINES

They are used when the patients are agitated and who develop seizures.

Diazepam appears to counteract some aspects of CNS derived symptoms which are not affected by atropine.Diazepam 10 mg slow IV push, repeated as necessary.Up to 30-40 mg diazepam per 24 hours can be given.

E) OTHER MEDICATIONS

a) **Magnesium** :It was thought to be counteracting the direct toxi inhibitory effect of OPC'c on N.K.Atase.Singh et al administered magnesium sulphate 4mg IV to patients intoxicated with OP and observed that the neuroeletrophysiological effects that had been observed earlier were reversed.

b) **Clonidine:**

- Protective effects of clonidine or likely to involve multiple effects including
- Blockade of acetylcholine release and post synaptic muscarinic receptors.
- Transient inhibition of acetylcholinesterase
- Inhibits the release of acetylcholine from central and peripheral cholinergic neurons.

MANAGEMENT OF INTERMEDIATE SYNDROME

It usually presents 12 to 96 hours after exposure. Early signs of intermediate syndrome are action tremors and pharyngeal weakness (difficulty in deglutition or pooling of secretions in pharynx).Later patient develops inability to flex neck, deep tendon jerks are lost, develop cranial neuropathies, proximal muscle weakness and respiratory muscle paralysis. Not all patients will develop the full intermediate syndrome requiring intubation and ventilation, but patients with tremors and pharyngeal weakness are at risk. Later patient develops inability to flex neck, deep tendon jerks are lost, develop cranial neuropathies, proximal muscle weakness and respiratory muscle paralysis. Treatment of intermediate syndrome totally symptomatic.

PAM should be continued and provide adequate ventilator support. Patient should be kept in hospital upto 5 days because patient may develop respiratory difficulty during the recovery phase of cholinergic crisis. During the intermediate syndrome patient may develop profuse diarrhea. They should be managed with fluids and electrolytes.

Patient will require ventilator support if he develops respiratory muscle paralysis. Do not use atropine unless signs of cholinergic excess are present. Common cause of death in Organophosphorus poisoning is respiratory failure and complication in management of respiratory failure.

MANAGEMENT OF DELAYED POLYNEUROPATHY

Physiotherapy and exercise done regularly may improve the muscle weakness. No drugs are available for treatment of this condition.

MORTALITY:

Mortality rate in India and other developing countries ranges from 4-38%.Mortality depends upon the poison used, quantity ,duration after exposure and atropinisation of all the toxins.

Malathion has the lowest toxicity because of rapid hydrolyzation of carboxy ester group to products with little or no anticholinesterase activity. Fenthion has the maximum mortality.

Early death is due to

1) CNS depression

2) Seizures

3) Ventricular arrhythmias

4) Respiratory failure due to

- Excessive bronchial secretions
- Bronchospasms
- Pulmonary oedema
- Paralysis of respiratory muscles

 Apnea due to depression of medullary respiratory center.

Late death is due to

1. Respiratory failure associated with

   Infection

   Pneumonia

   Septicaemia

2. Complication due to mechanical ventilation

3. Ventricular arrythymias ,sudden collapse.

PATHOPHYSIOLOGY OF SERUM CREATINE PHOSPHOKINASE

Experimental study done in rats with an OP showed decrease in tissues ChE activity accompanied by increase in serum CPK activity. The CPK activity was significantly elevated in poisoning cases and more significant changes in the patients who died due to poisoning. Significant increase in serum creatine phosphokinase coincides with the appearance of myonecrosis , destruction of musclemembrane. The initial changes are in the mitochondria, which swell and then show lysis of the central cristae.

Though there is difference in structures of these AChEIs, the imyopathic changes which is induced is same, suggesting that it is a common mechanism. This mechanism is due to an excess of Ach and its interactions with nAChRs and it is not a direct action of these inhibitors on muscle. The common denominator is muscle hyperactivity, such as fasciculations.

Carbofuran cause fasciculations and myopathy produces a significant increase in serum total CK activity that was seen as early as half an hour after carbofuran injection and persistedly increasing for 3hrs. Under influenceof acute carbofuran poisoning , examination of the serum and diaphragm revealed several characteristic changesin CK isoenzymes. Theisoezyme CK-MM type was elevated >2 fold in the diaphragm within half an hour and remained significantly higher than control at 24hr. The leakage of CK decreased following restoration of normal muscle activity.

MATERIALS AND METHODS

MATERIALS AND METHODS

- **Study centre** : Toxicology ward, Institute of Internal Medicine MMC, RGGGH
- **Duration of study** : 6 months (From November 2017 to April 2018)
- **Study design** : Observational study
- **Sample Size** : 100 patients
- **Analysis Plan** : SPSS, Epi info
- **Inclusion Criteria**

All cases of acute organophosphorus poisoning admitted to our hospital within 24 hours with clinical features and physical evidence of consumption of the poison irrespective of age and gender.

- **Exclusion Criteria**

1. Consumption of Organophosphorous poison with alcohol .
2. Other pesticide poisoning.
3. Mixed poisoning.
4. Other routes of ingestion (skin, ear and eye)
5. Known medical illness like chronic liver disease, malignancy, renal failure, myopathy, autoimmune disorder, coronary artery disease

6. Patients on drugs like aspirin, statins, steroids, analgesics, ocps.

7. Patients with lipid disorders and gall stone diseases

❖ **Methodology :**

After obtaining the informed consent details of history and clinical examination were recorded. Peradeniya OP poisoning scale was applied to all study subjects and the severity of OP poisoning was graded as mild, moderate, severe. In all study subjects blood was collected on admission, day 2, day of discharge for estimation of serum amylase, lipase, acetyl cholinesterase and creatine phosphokinase. Other routine investigations were done.

❖ **Statistical analysis:**

1. Continuous variables are represented in mean, median, mode and standard deviation.
2. Categorical variables are represented in frequencies and percentages.
3. When a Categorical Variable is associated with a categorical variable, the variables are represented in both by tables and bar diagrams. For test of significance, chi-square test is used. Fisher's exact test is used when more than 20% of the cell values have expected cell value less than 5.
4. When a continuous variable is associated with continuous variable, correlation tests are used.
5. When the paired samples variable such as variable at admission, day one and at discharge is associated with the categorical variables such

as outcome, clinical severity, and then repeated measures ANOVA is used.

6. P-value less than 0.05 is considered statistically significant.
7. Data was analysed using SPSS software version 16.

RESULTS

OBSERVATION AND RESULTS

RESULTS

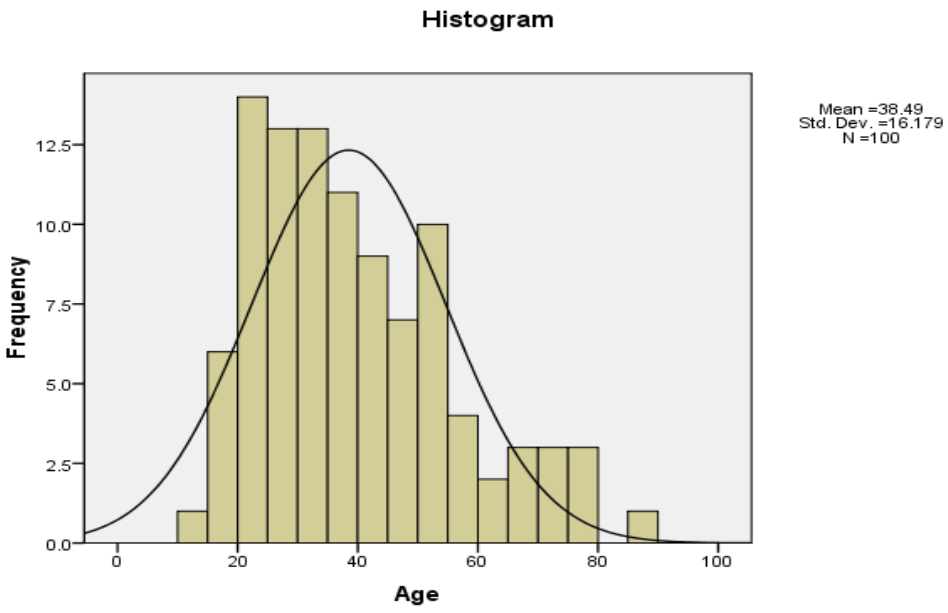
1) Population Characteristics:

A) Age:

The mean age of the study population was 38.49 and standard deviation of 16.17. This is represented in the following table.

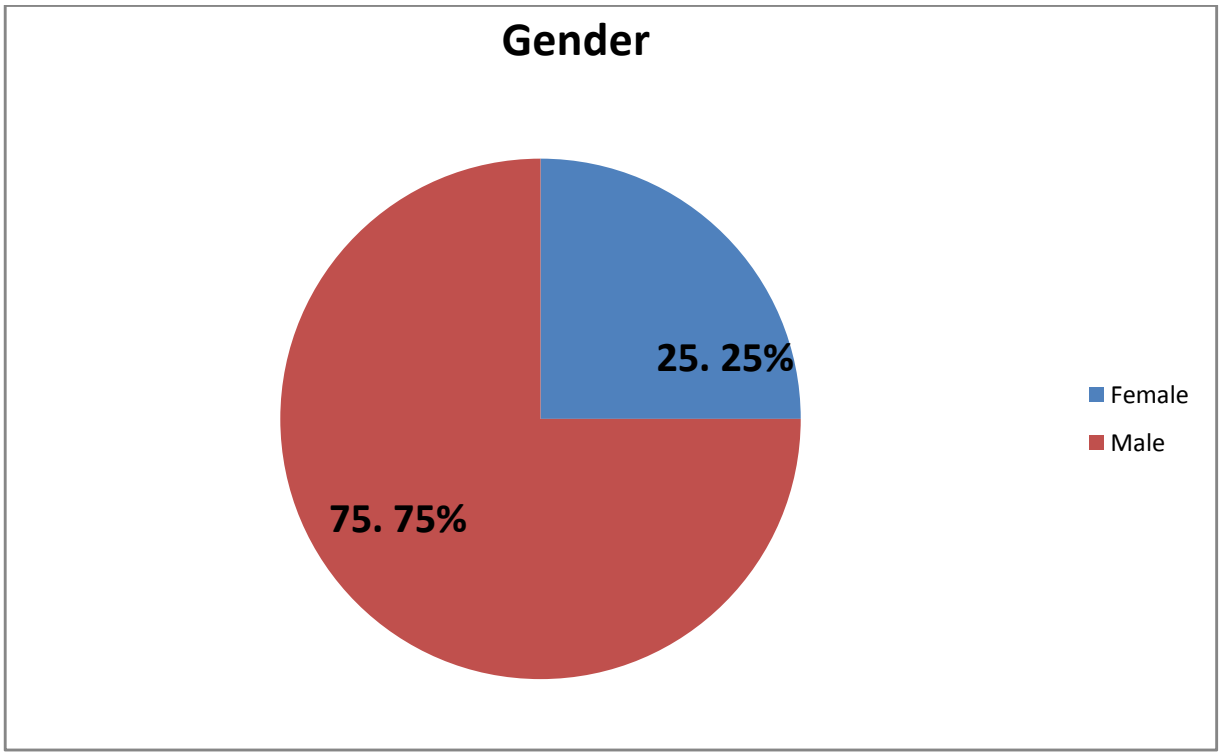
Mean	38.49
Median	35.00
Mode	50
Std. Deviation	16.179
Minimum	14
Maximum	85

The Following Histogram shows the distribution of age in the study population:



B) Gender:

The study population comprised of 25% females and 75% males. And this is represented in the following Pie-chart.

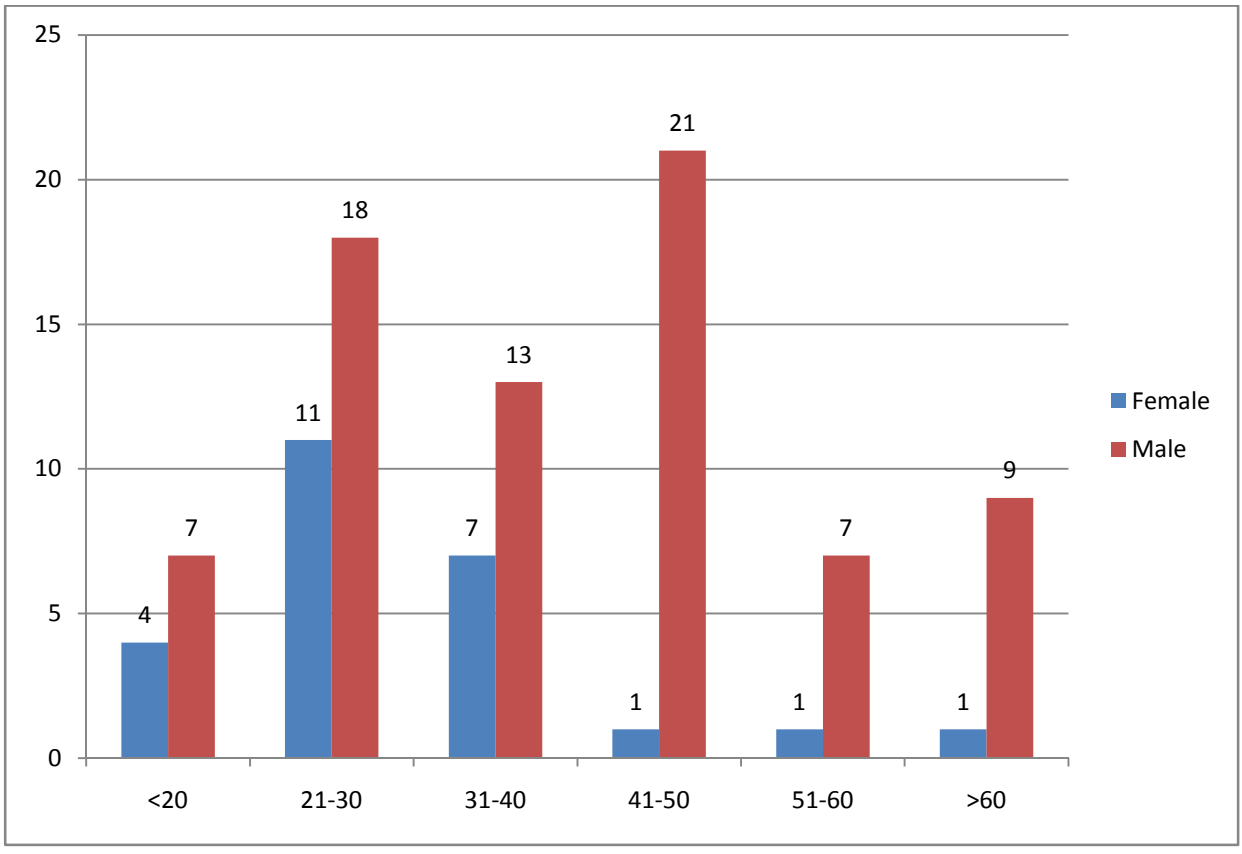


C) Age and Sex Distribution:

			Sex		Total
			F	M	
Age category (Years)	<20	Count	4	7	11
		% within Age	36.4 %	63.6 %	100.0%
	21-30	Count	11	18	29
		% within Age	37.9 %	62.1 %	100.0%
	31-40	Count	7	13	20
		% within Age	35.0 %	65.0 %	100.0%
	41-50	Count	1	21	22

		% within Age	4.5%	95.5 %	100.0%
	51-60	Count	1	7	8
		% within Age	12.5 %	87.5 %	100.0%
	>60	Count	1	9	10
		% within Age	10.0 %	90.0 %	100.0%
Total		Count	25	75	100
		% within Age	25.0 %	75.0 %	100.0%

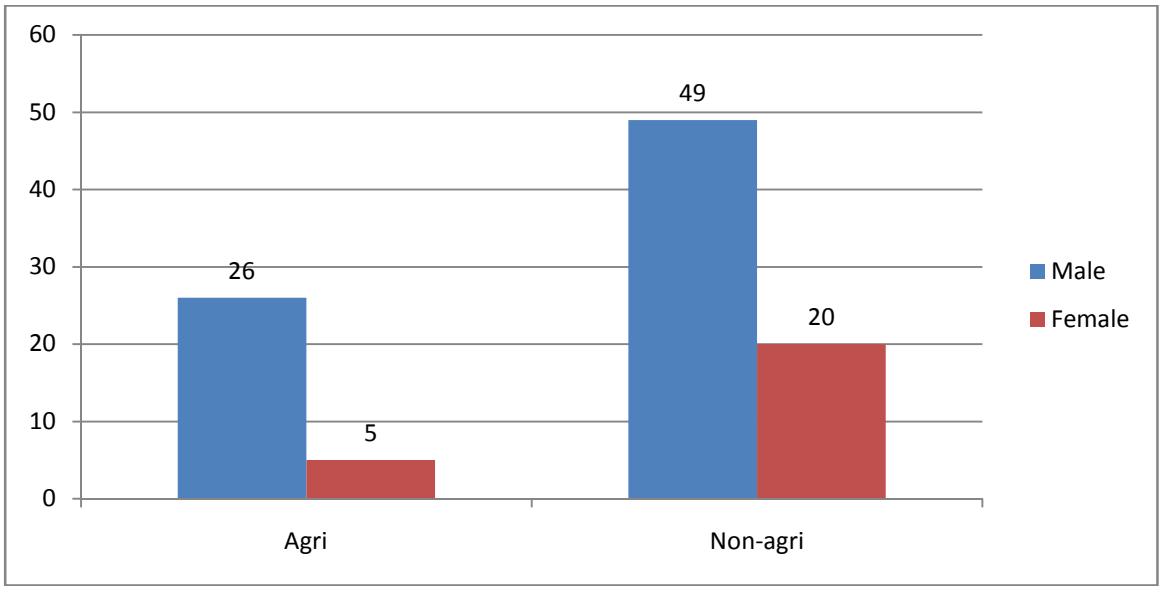
Bar Diagram (Age in Yrs. In X axis & No. of Persons in Y axis with Males and Females in the graph)



2) Occupation:

			Sex		Total
			F	M	
Occupation	Agri	Count	5	26	31
		% within Occupation	16.1%	83.9%	100.0%
	Non-Agri	Count	20	49	69
		% within Occupation	29.0%	71.0%	100.0%
Total		Count	25	75	100
		% within Occupation	25.0%	75.0%	100.0%

Bar Diagram (Frequency in X axis with Agri& Non-Agri with Male & Female in the graph with No. of Persons in Y axis)

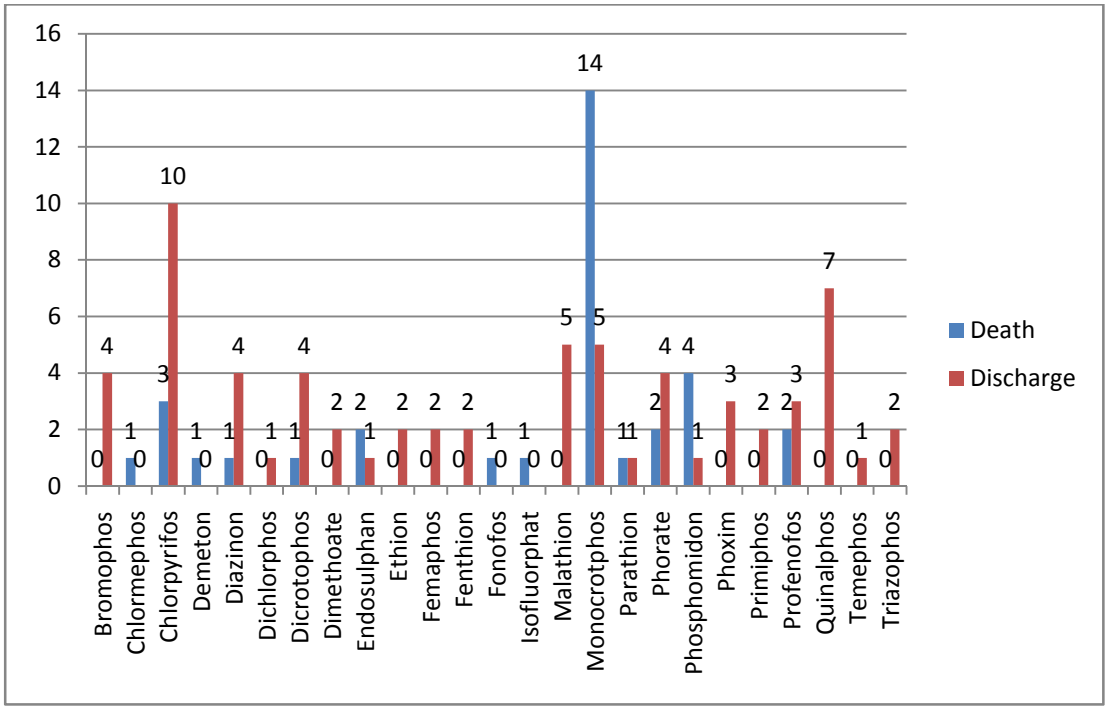


3) Types of Compound and Outcome

			Outcome		
			Death	Discharge	Total
Compound	Bromophos	Count	0	4	4
		% within Compound	.0%	100.0%	100.0%
	Chlormephos	Count	1	0	1
		% within Compound	100.0%	.0%	100.0%
	Chlorpyrifos	Count	3	10	13
		% within Compound	23.1%	76.9%	100.0%
	Demeton	Count	1	0	1
		% within Compound	100.0%	.0%	100.0%
	Diazinon	Count	1	4	5
		% within Compound	20.0%	80.0%	100.0%
	Dichlorphos	Count	0	1	1
		% within Compound	.0%	100.0%	100.0%
	Dicrotophos	Count	1	4	5
		% within Compound	20.0%	80.0%	100.0%
	Dimethoate	Count	0	2	2
		% within Compound	.0%	100.0%	100.0%
	Endosulphan	Count	2	1	3
		% within Compound	66.7%	33.3%	100.0%
	Ethion	Count	0	2	2
		% within Compound	.0%	100.0%	100.0%
	Femaphos	Count	0	2	2
		% within Compound	.0%	100.0%	100.0%
	Fenthion	Count	0	2	2
		% within Compound	.0%	100.0%	100.0%
	Fonofos	Count	1	0	1
		% within Compound	100.0%	.0%	100.0%
	Isofluorphat	Count	1	0	1
		% within Compound	100.0%	.0%	100.0%
	Malathion	Count	0	5	5
		% within Compound	.0%	100.0%	100.0%

	Monocrotphos	Count	14	5	19
		% within Compound	73.7%	26.3%	100.0%
	Parathion	Count	1	1	2
		% within Compound	50.0%	50.0%	100.0%
	Phorate	Count	2	4	6
		% within Compound	33.3%	66.7%	100.0%
	Phosphomidon	Count	4	1	5
		% within Compound	80.0%	20.0%	100.0%
	Phoxim	Count	0	3	3
		% within Compound	.0%	100.0%	100.0%
	Primiphos	Count	0	2	2
		% within Compound	.0%	100.0%	100.0%
	Profenofos	Count	2	3	5
		% within Compound	40.0%	60.0%	100.0%
	Quinalphos	Count	0	7	7
		% within Compound	.0%	100.0%	100.0%
	Temephos	Count	0	1	1
		% within Compound	.0%	100.0%	100.0%
	Triazophos	Count	0	2	2
		% within Compound	.0%	100.0%	100.0%
Total		Count	34	66	100
		% within Compound	34.0%	66.0%	100.0%

Fisher’s Exact value = 40.587 p-Value =0.001Bar Diagram (Types of Compound In X axis & No. of cases in Y axis with Discharge and Death)



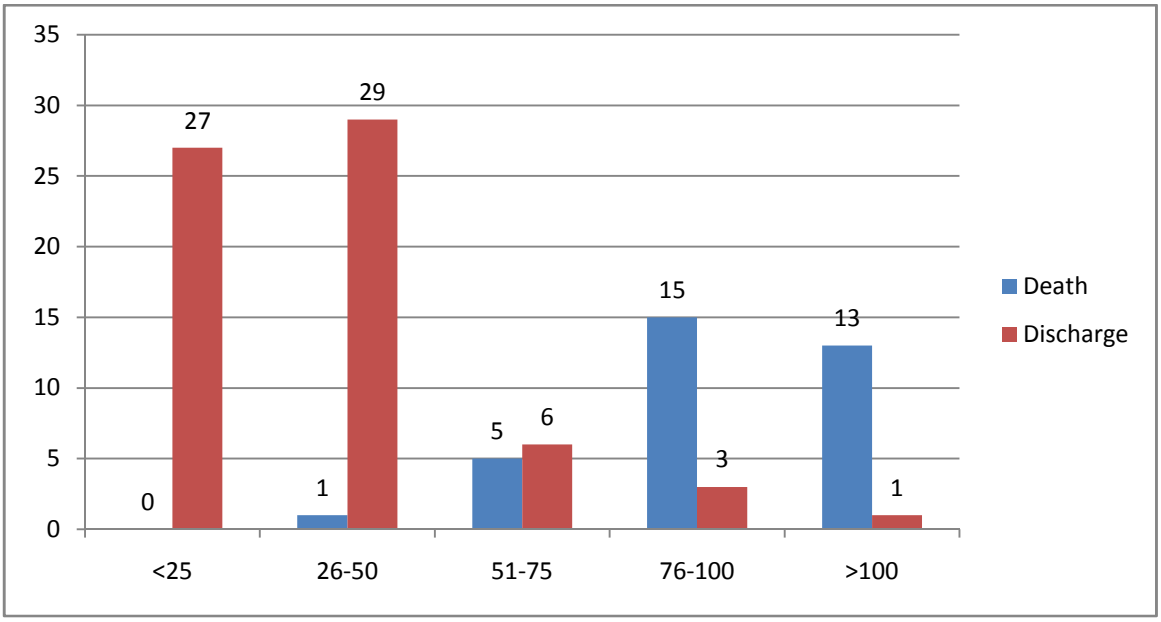
4) Quantity of Exposure and Outcome:

Mean	63.55
Median	50.00
Mode	25
Std. Deviation	44.006
Minimum	10
Maximum	150

			Outcome		Total
			Death	Discharge	
Quantity (ml)	<25	Count	0	27	27
		% within Quantcate	.0%	100.0%	100.0%
	26-50	Count	1	29	30
		% within Quantcate	3.3%	96.7%	100.0%

	51-75	Count	5	6	11
		% within Quantcate	45.5%	54.5%	100.0%
	76-100	Count	15	3	18
		% within Quantcate	83.3%	16.7%	100.0%
	>100	Count	13	1	14
		% within Quantcate	92.9%	7.1%	100.0%
Total		Count	34	66	100
		% within Quantcate	34.0%	66.0%	100.0%

Bar Diagram (Quantity in ml in X axis and No. of cases in Y axis with Death and Discharge).

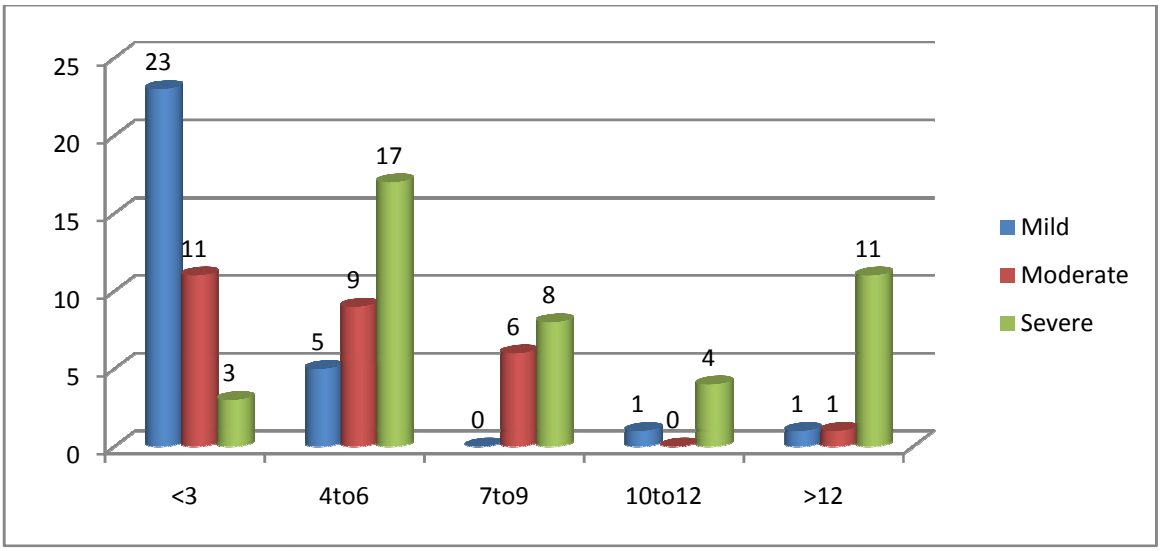


5) Duration of Presentation and Clinical Severity by POP score

			POP Score			Total
			Mild	Moderate	Severe	
Duration	<3	Count	23	11	3	37
		% within durcat	62.2%	29.7%	8.1%	100.0%
	4-6	Count	5	9	17	31
		% within durcat	16.1%	29.0%	54.8%	100.0%
	7-9	Count	0	6	8	14
		% within durcat	.0%	42.9%	57.1%	100.0%
	10-12	Count	1	0	4	5
		% within durcat	20.0%	.0%	80.0%	100.0%
	>12	Count	1	1	11	13
		% within durcat	7.7%	7.7%	84.6%	100.0%
Total		Count	30	27	43	100
		% within durcat	30.0%	27.0%	43.0%	100.0%

Fisher's Exact Test Value = 46 p-value= <0.001

Bar diagram (No.of Hours in X axis with No. of cases in Y axis with Mild, Moderate and Severe in the graph)

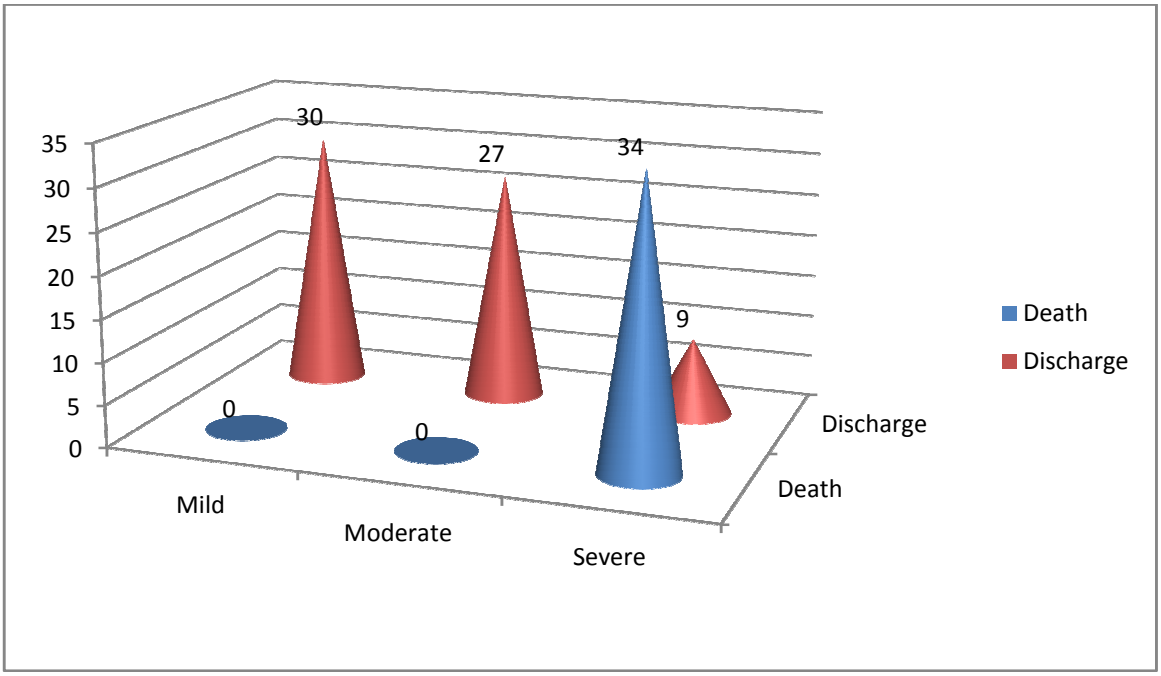


6) Clinical Severity by POP Score and Outcome

			Outcome		Total
			Death	Discharge	
POP score	Mild	Count	0	30	30
		% within popscore	.0%	100.0%	100.0%
	Moderate	Count	0	27	27
		% within popscore	.0%	100.0%	100.0%
	Severe	Count	34	9	43
		% within popscore	79.1%	20.9%	100.0%
Total		Count	34	66	100
		% within popscore	34.0%	66.0%	100.0%

Chi-Square test value = 68 p-value=<0.001

Bar Diagram (POP Score with Mild, Moderate, Severe & Total in X axis with number of cases in Y axis) :

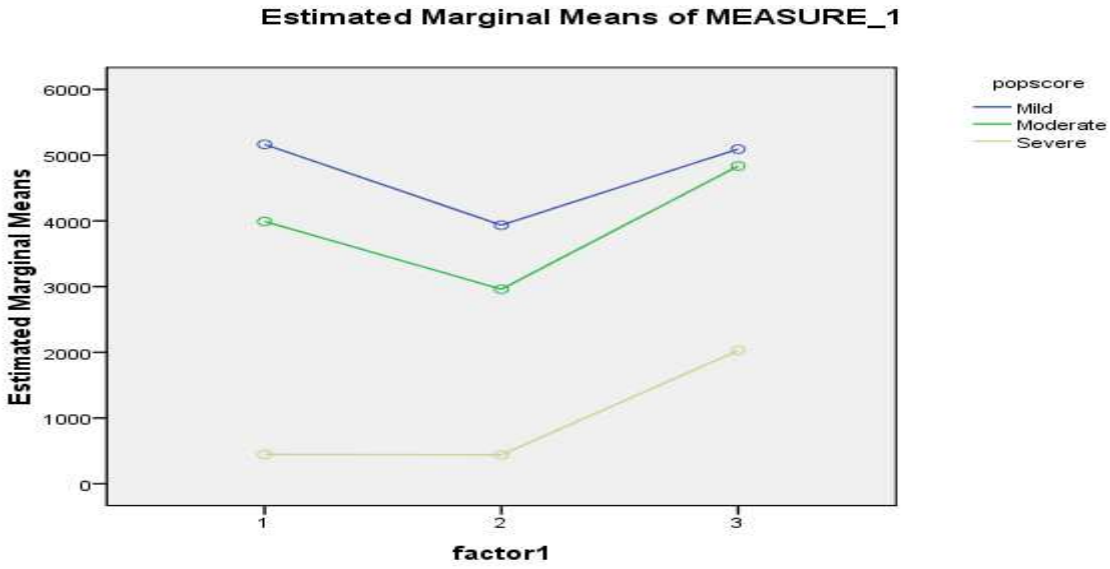


7) Clinical Severity and Mean Acetyl Cholinesterase (AchE) values

	POP score	Mean	Std. Deviation	N
Ach Day 1	Mild	5163.70	2141.799	30
	Moderate	3990.96	2185.931	27
	Severe	447.77	365.618	31
	Total	3142.59	2687.519	88
Ach Day 2	Mild	3934.77	1083.934	30
	Moderate	2959.89	1028.229	27
	Severe	439.61	328.203	31
	Total	2404.41	1738.862	88
Ach Discharge	Mild	5092.03	1138.736	30
	Moderate	4833.81	801.782	27
	Severe	2025.97	1290.781	31
	Total	3932.72	1791.592	88

p-Value<0.001 (Repeated Measures ANOVA Used)

Line diagram (Mild, Moderate & Severe POP score in X axis with AchE values in Y axis)

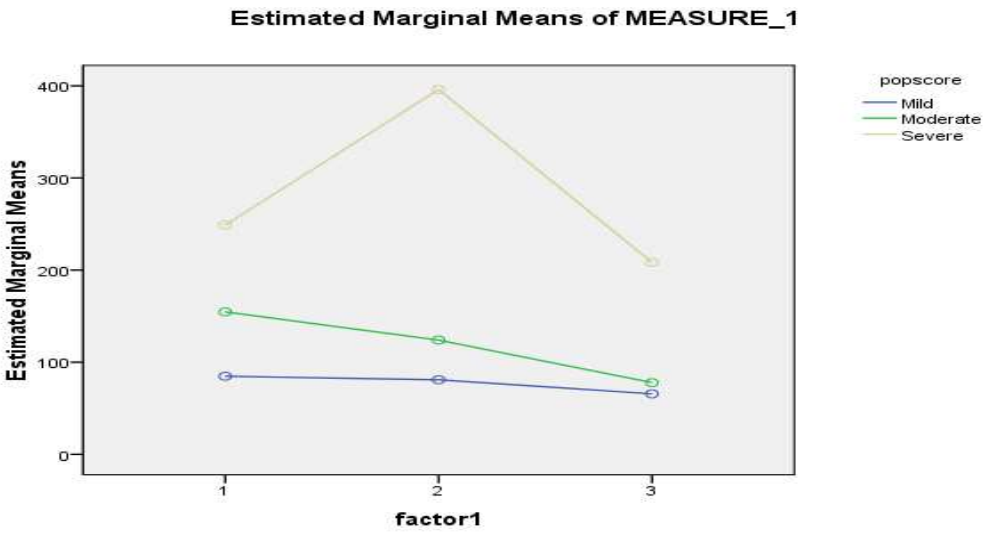


8) Clinical Severity and Mean Serum Amylase:

	POP score	Mean	Std. Deviation	N
Amylase Day 1	Mild	84.73	48.225	30
	Moderate	154.59	131.818	27
	Severe	248.94	147.786	31
	Total	164.01	135.144	88
Amylase Day 2	Mild	80.93	49.373	30
	Moderate	124.00	80.139	27
	Severe	396.03	309.277	31
	Total	205.15	236.775	88
Amylase Discharge	Mild	65.63	18.365	30
	Moderate	77.85	22.300	27
	Severe	208.42	179.641	31
	Total	119.68	125.479	88

p-Value<0.001 (Repeated Measures ANOVA Used)

Bar Diagram (Mild, Moderate & Severe in X axis with Values in Y axis with Amylase)

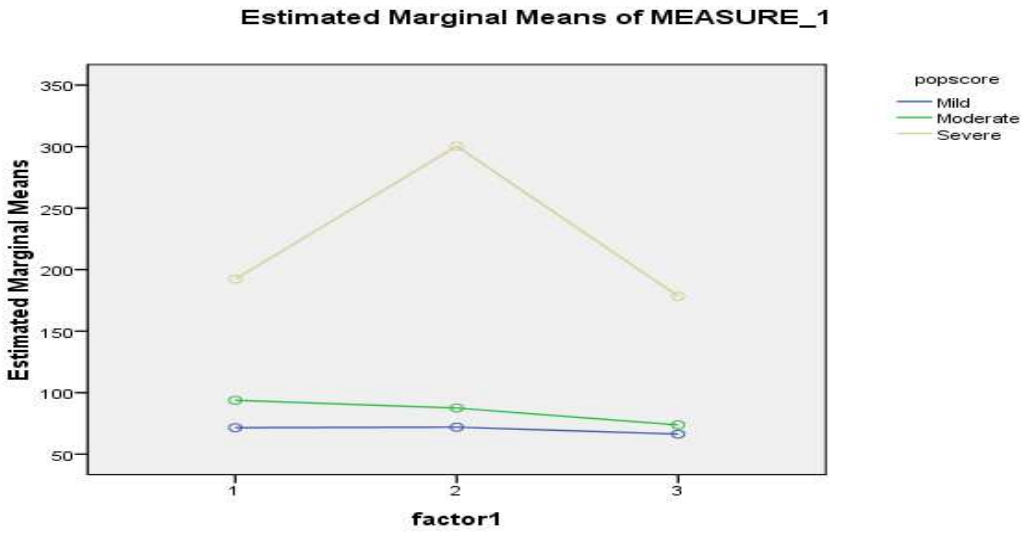


9) Clinical Severity and Mean Serum Lipase:

	POP score	Mean	Std. Deviation	N
Lipase Day 1	Mild	71.53	17.716	30
	Moderate	93.78	49.825	27
	Severe	192.26	105.996	31
	Total	120.89	87.199	88
Lipase Day 2	Mild	71.93	20.794	30
	Moderate	87.48	37.286	27
	Severe	300.35	242.141	31
	Total	157.17	179.152	88
Lipase Discharge	Mild	66.30	14.408	30
	Moderate	73.74	19.542	27
	Severe	178.32	154.783	31
	Total	108.05	105.691	88

p-Value = 0.007 (Repeated Measures ANOVA Used)

Line Diagram (Mild, Moderate & Severe in X axis with Values in Y axis with Lipase)

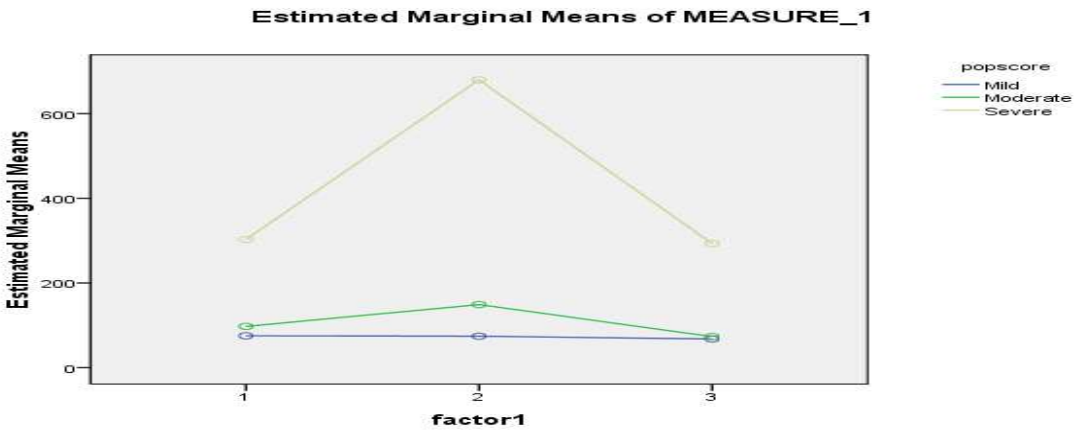


10) Clinical Severity and Mean creatine Kinase:

	Popscore	Mean	Std. Deviation	N
CK Day 1	Mild	75.17	38.930	30
	Moderate	97.44	82.926	27
	Severe	302.84	211.099	31
	Total	162.20	169.965	88
CK Day 2	Mild	74.30	30.005	30
	Moderate	148.93	243.244	27
	Severe	679.71	595.233	31
	Total	310.47	464.831	88
CK Discharge	Mild	67.67	23.527	30
	Moderate	73.41	27.057	27
	Severe	293.16	331.573	31
	Total	148.86	223.100	88

p-Value< 0.001 (Repeated Measures ANOVA Used)

Line Diagram (Mild, Moderate & Severe in X axis with Values in Y axis with Creatine Kinase)



11) Correlation between Duration of Presentation and AchE values, Serum Amylase, Lipase & CK values:

		duration	quantity	hospstay	Atropine dose
Ach Day 1	Pearson Correlation	-.390**	-.692**	-.199*	-.554**
	Sig. (2-tailed)	.000	.000	.047	.000
	N	100	100	100	100
Ach Day 2	Pearson Correlation	-.461**	-.777**	-.386**	-.620**
	Sig. (2-tailed)	.000	.000	.000	.000
	N	92	92	92	92
Ach Discharge	Pearson Correlation	-.430**	-.733**	-.123	-.454**
	Sig. (2-tailed)	.000	.000	.255	.000
	N	88	88	88	88
Amylase Day 1	Pearson Correlation	.192	.490**	.008	.302**
	Sig. (2-tailed)	.056	.000	.941	.002
	N	100	100	100	100
Amylase Day 2	Pearson Correlation	.159	.426**	.343**	.435**
	Sig. (2-tailed)	.131	.000	.001	.000
	N	92	92	92	92
Amylase Discharge	Pearson Correlation	.318**	.480**	.016	.316**
	Sig. (2-tailed)	.002	.000	.882	.003
	N	88	88	88	88
Lipase Day 1	Pearson Correlation	.265**	.555**	.017	.311**
	Sig. (2-tailed)	.008	.000	.866	.002
	N	100	100	100	100
Lipase Day 2	Pearson Correlation	.118	.446**	.424**	.472**
	Sig. (2-tailed)	.264	.000	.000	.000
	N	92	92	92	92
Lipase Discharge	Pearson Correlation	.312**	.452**	.016	.287**
	Sig. (2-tailed)	.003	.000	.880	.007
	N	88	88	88	88
CK Day 1	Pearson Correlation	.328**	.529**	.161	.506**
	Sig. (2-tailed)	.001	.000	.111	.000
	N	100	100	100	100

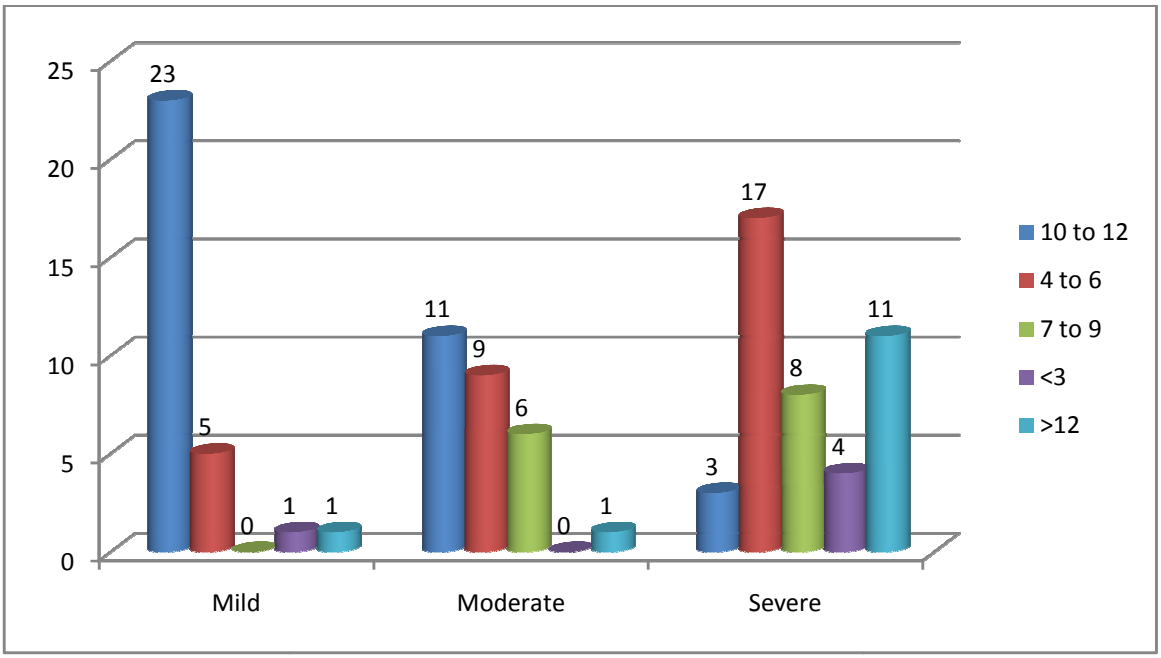
CK Day 2	Pearson Correlation	.214*	.443**	.556**	.668**
	Sig. (2-tailed)	.041	.000	.000	.000
	N	92	92	92	92
CK Discharge	Pearson Correlation	.342**	.462**	-.007	.320**
	Sig. (2-tailed)	.001	.000	.945	.002
	N	88	88	88	88
**. Correlation is significant at the 0.01 level (2-tailed).					
*. Correlation is significant at the 0.05 level (2-tailed).					

12) Clinical severity and duration of hospital stay:

			Hospital Stay Duration (Days)					
			10-12	4-6	7-9	<3	>12	Total
POP score	Mild	Count	1	5	0	23	1	30
		% within POPscore	3.3%	16.7%	.0%	76.7%	3.3%	100.0%
	Moderate	Count	0	9	6	11	1	27
		% within POPscore	.0%	33.3%	22.2%	40.7%	3.7%	100.0%
	Severe	Count	4	17	8	3	11	43
		% within POPscore	9.3%	39.5%	18.6%	7.0%	25.6%	100.0%
Total		Count	5	31	14	37	13	100
		% within POPscore	5.0%	31.0%	14.0%	37.0%	13.0%	100.0%

Pearson's Chi Square Value = 44.8 p-Value=<0.001

Bar diagram (Duration of hospital stay (days) in X axis with Mild, Moderate & Severe Score and no.of persons in Y axis)

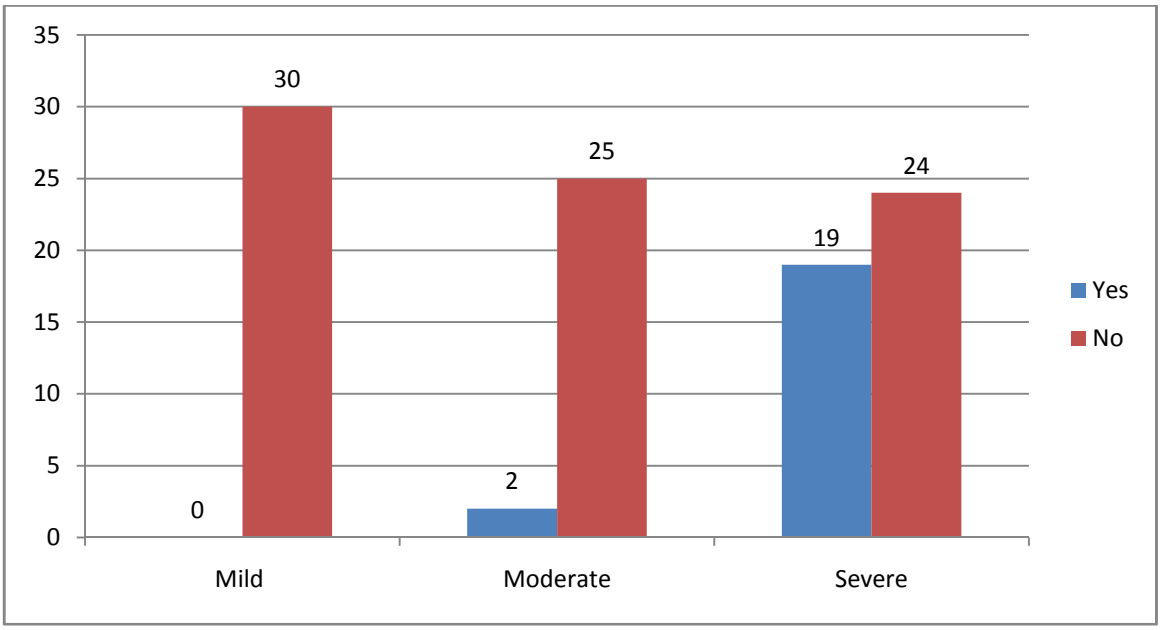


13) Intermediate syndrome (IMS) and Clinical Severity:

			IMS		Total
			No	Yes	
POP score	Mild	Count	30	0	30
		% within popscore	100.0%	.0%	100.0%
	Moderate	Count	25	2	27
		% within popscore	92.6%	7.4%	100.0%
	Severe	Count	24	19	43
		% within popscore	55.8%	44.2%	100.0%
Total		Count	79	21	100
		% within popscore	79.0%	21.0%	100.0%

Pearson's Chi-Square test value 24.9 p-Value = <0.001

Bar diagram Intermediate syndrome in X axis with Clinical Severity (mild, Moderate & Severe Score) and no.of persons in Y axis:

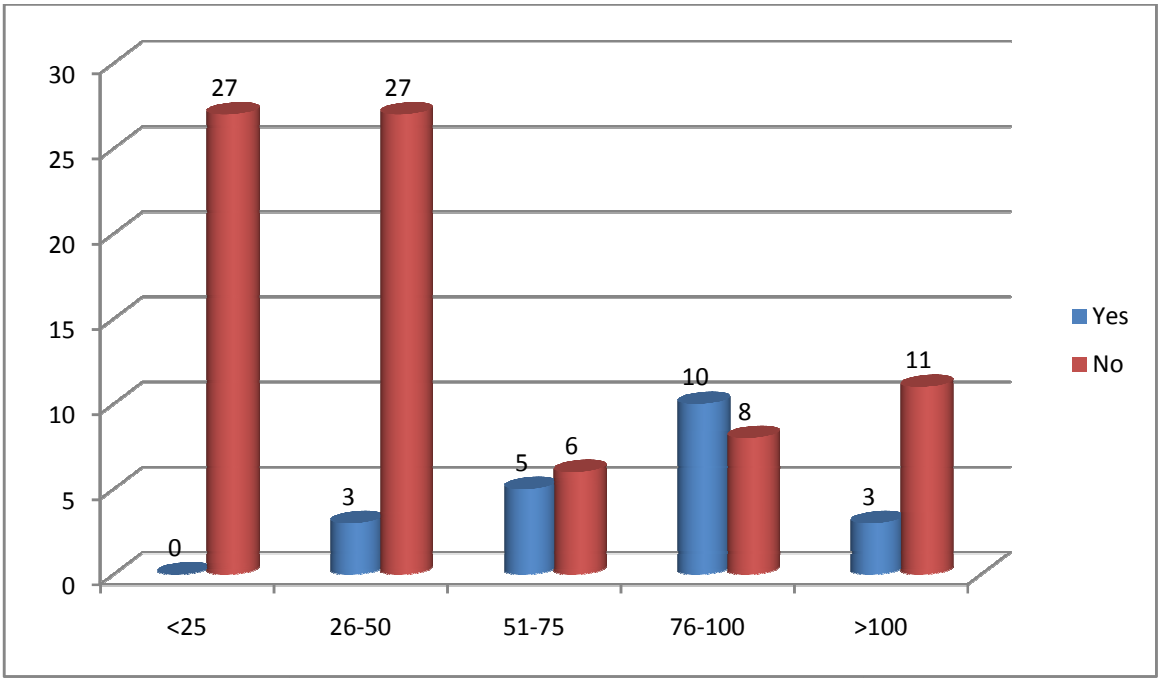


14) Intermediate Syndrome and Quantity of Exposure:

			IMS		Total
			No	Yes	
Quantity (ml)	26-50	Count	27	3	30
		% within Quantcate	90.0%	10.0%	100.0%
	51-75	Count	6	5	11
		% within Quantcate	54.5%	45.5%	100.0%
	76-100	Count	8	10	18
		% within Quantcate	44.4%	55.6%	100.0%
	<25	Count	27	0	27
		% within Quantcate	100.0%	.0%	100.0%
	>100	Count	11	3	14
		% within Quantcate	78.6%	21.4%	100.0%
Total		Count	79	21	100
		% within Quantcate	79.0%	21.0%	100.0%

Chi-square value = 26.2 p-value= <0.001

Bar Diagram showing Intermediate Syndrome and Quantity of Exposure:

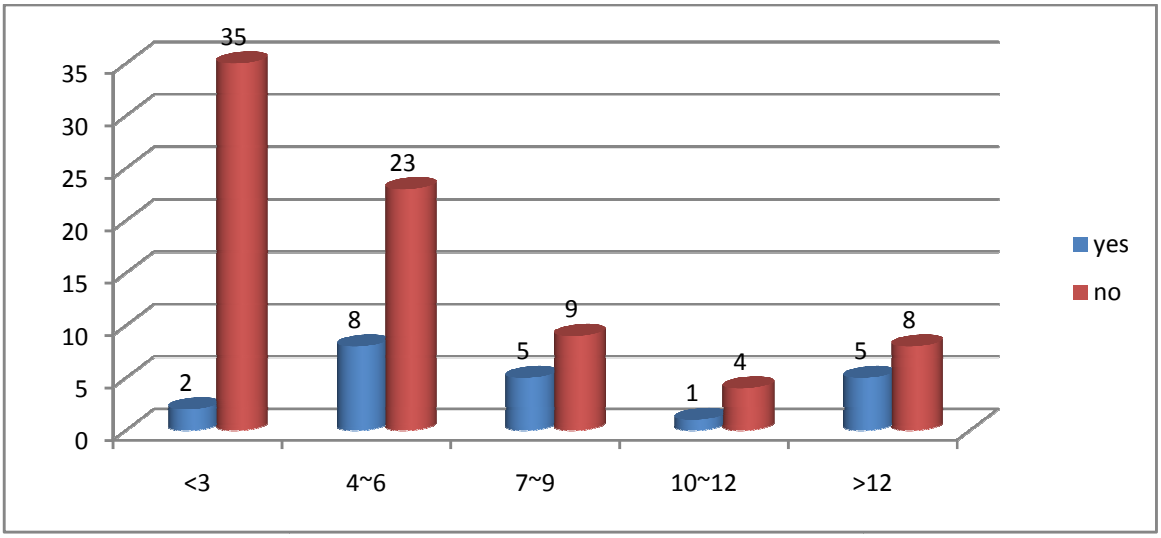


15) Intermediate syndrome and duration of exposure:

			IMS		Total
			No	Yes	
Duration (Days)	10-12	Count	4	1	5
		% within durcat	80.0%	20.0%	100.0%
	4-6	Count	23	8	31
		% within durcat	74.2%	25.8%	100.0%
	7-9	Count	9	5	14
		% within durcat	64.3%	35.7%	100.0%
	<3	Count	35	2	37
		% within durcat	94.6%	5.4%	100.0%
	>12	Count	8	5	13
		% within durcat	61.5%	38.5%	100.0%
Total		Count	79	21	100
		% within durcat	79.0%	21.0%	100.0%

Fisher's Exact Test value =11.210 p-value = 0.015

Bar diagram showing Intermediate syndrome and duration of exposure:

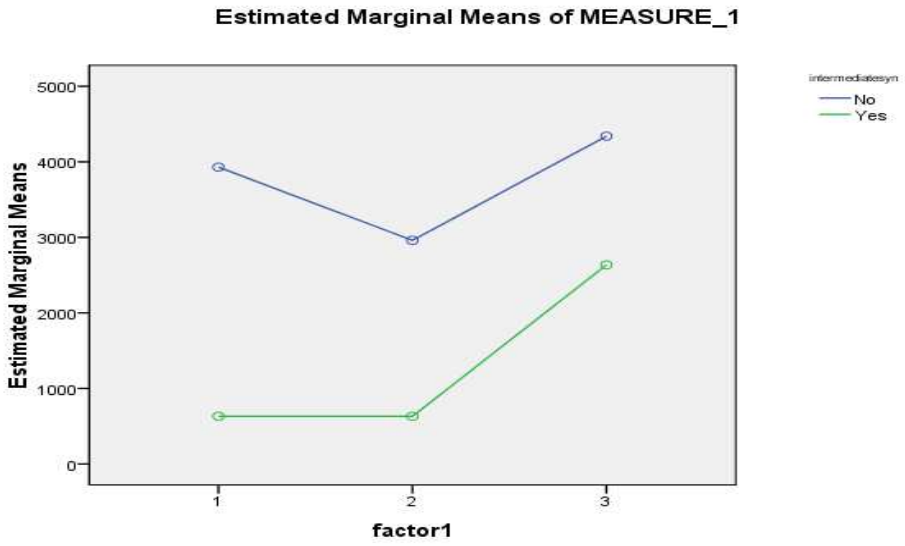


16) Intermediate syndrome and Acetylcholine esterase level:

IMS		Mean	Std. Deviation	N
Ach Day 1	No	3929.67	2569.184	67
	Yes	631.43	969.604	21
	Total	3142.59	2687.519	88
Ach Day 2	No	2960.37	1566.989	67
	Yes	630.62	843.035	21
	Total	2404.41	1738.862	88
Ach Discharge	No	4339.42	1607.861	67
	Yes	2635.14	1763.359	21
	Total	3932.72	1791.592	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Intermediate syndrome and Mean Acetyl choline esterase level at admission, day two and at discharge:

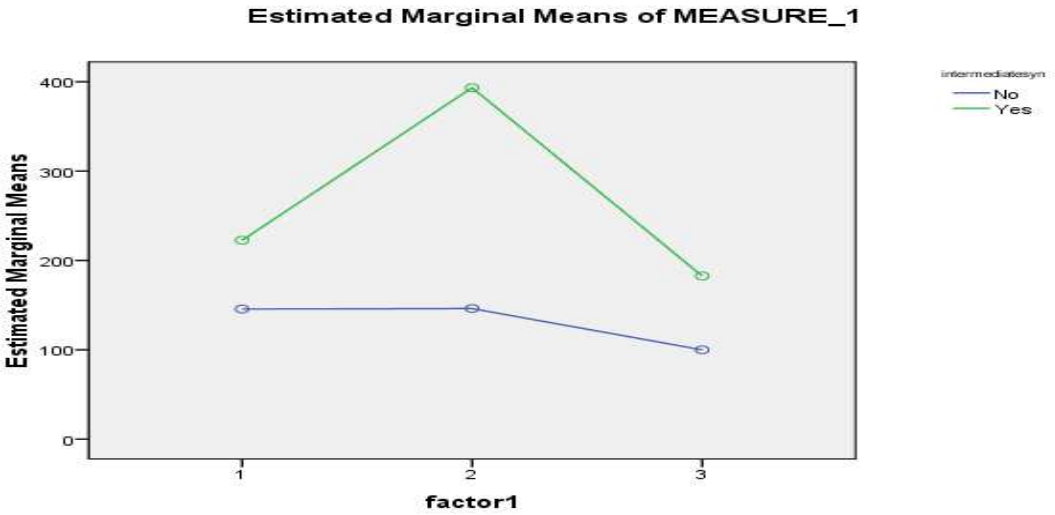


17) Intermediate syndrome and Serum Amylase level:

	IMS	Mean	Std. Deviation	N
Amylase Day 1	No	145.66	131.108	67
	Yes	222.57	134.142	21
	Total	164.01	135.144	88
Amylase Day 2	No	146.16	157.566	67
	Yes	393.33	336.309	21
	Total	205.15	236.775	88
Amylase Discharge	No	99.94	108.138	67
	Yes	182.67	156.303	21
	Total	119.68	125.479	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Intermediate syndrome and Mean Serum amylase level at admission, day two and at discharge:

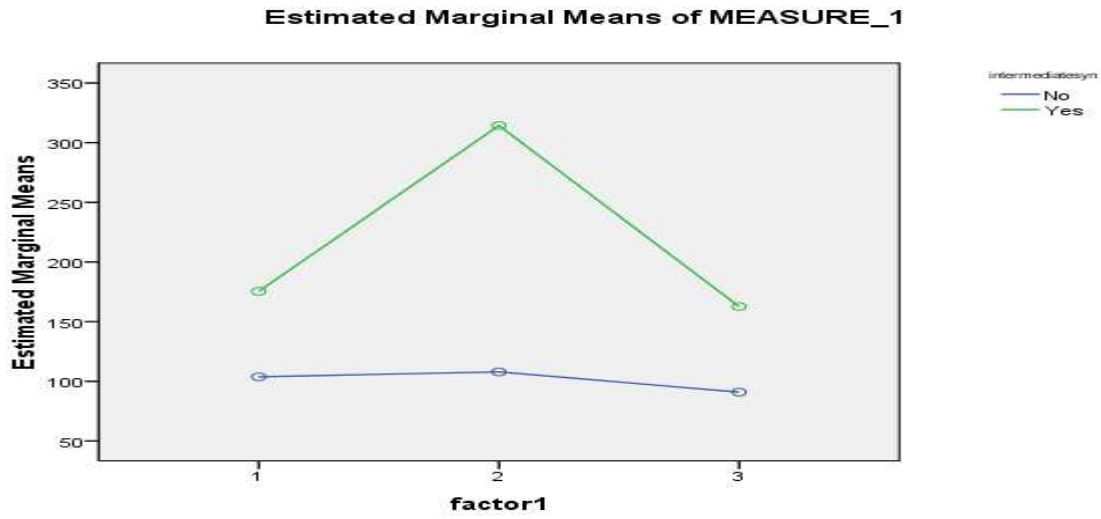


18) Intermediate syndrome and Lipase level:

	IMS	Mean	Std. Deviation	N
Lipase Day 1	No	103.79	76.361	67
	Yes	175.43	98.647	21
	Total	120.89	87.199	88
Lipase Day 2	No	107.91	95.075	67
	Yes	314.33	275.176	21
	Total	157.17	179.152	88
Lipase Discharge	No	90.93	86.872	67
	Yes	162.67	139.904	21
	Total	108.05	105.691	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Intermediate syndrome and Mean Serum lipase level at admission, day two and at discharge:

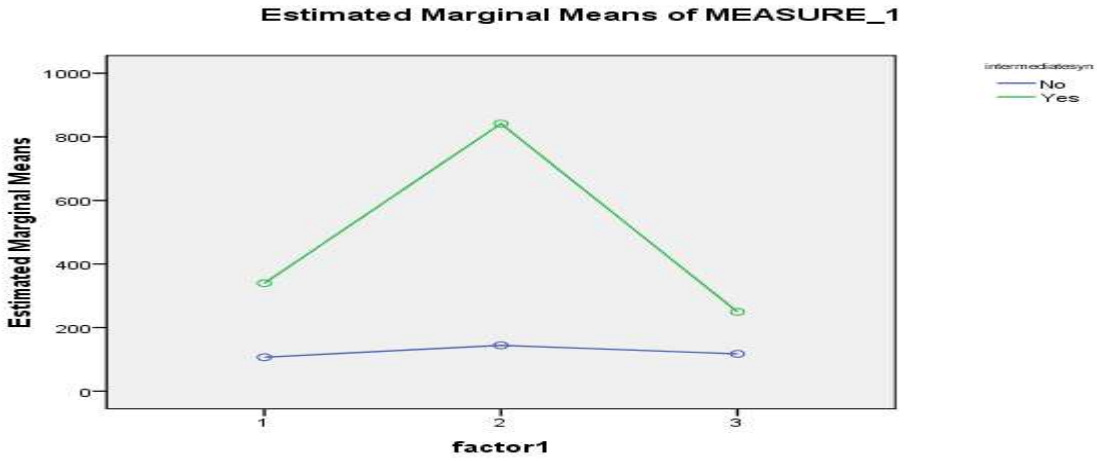


19) Intermediate syndrome and Creatine Kinase level:

	IMS	Mean	Std. Deviation	N
CK Day 1	No	106.61	100.626	67
	Yes	339.57	221.049	21
	Total	162.20	169.965	88
CK Day 2	No	144.07	237.895	67
	Yes	841.33	603.718	21
	Total	310.47	464.831	88
CK Discharge	No	117.34	205.632	67
	Yes	249.43	251.054	21
	Total	148.86	223.100	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Intermediate syndrome and Mean creatine Kinase level at admission, day two and at discharge:

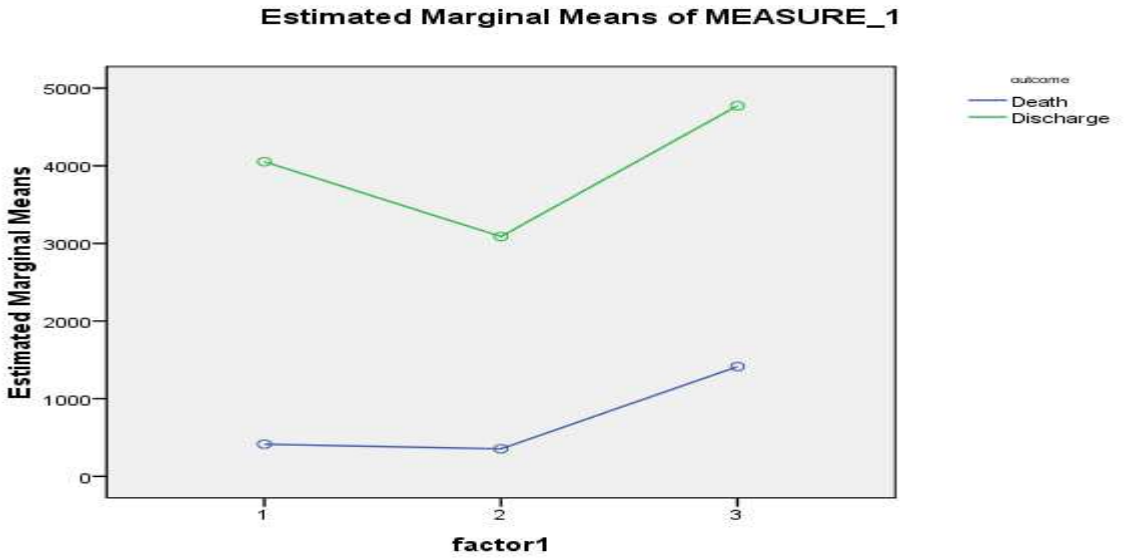


20) Outcome of the disease and mean Acetylcholine esterase level:

	outcome	Mean	Std. Deviation	N
AchE Day 1	Death	413.27	371.123	22
	Discharge	4052.36	2502.241	66
	Total	3142.59	2687.519	88
AchE Day 2	Death	353.68	146.535	22
	Discharge	3087.98	1463.636	66
	Total	2404.41	1738.862	88
AchE Discharge	Death	1413.36	838.515	22
	Discharge	4772.50	1097.584	66
	Total	3932.72	1791.592	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Outcome of the disease and Mean acetyl choline esterase level at admission, day two and at discharge:

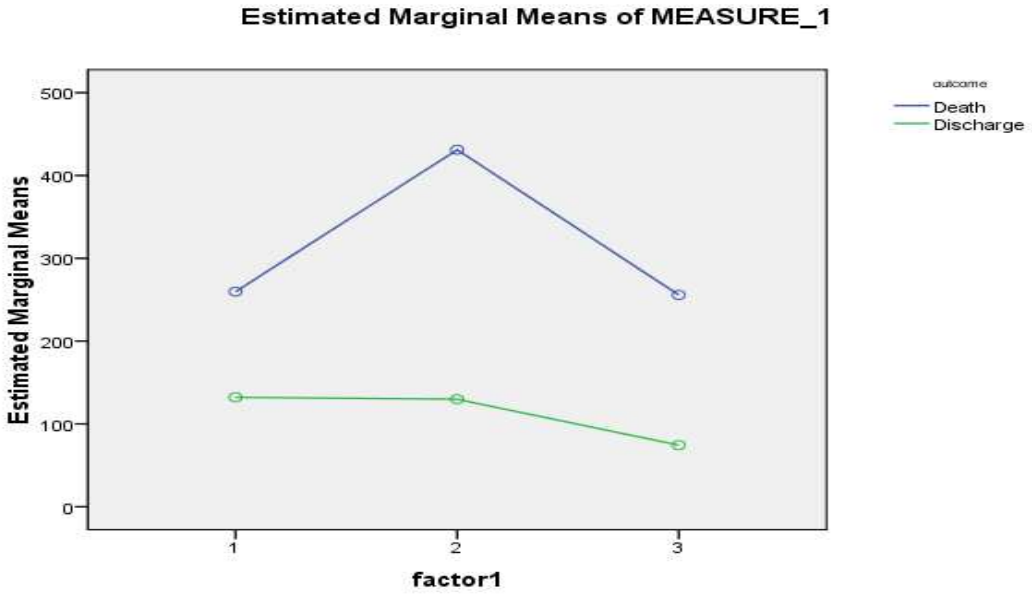


21) Outcome of the disease and mean amylase level:

	Outcome	Mean	Std. Deviation	N
Amylase Day 1	Death	259.68	139.300	22
	Discharge	132.12	118.515	66
	Total	164.01	135.144	88
Amylase Day 2	Death	431.09	316.957	22
	Discharge	129.83	139.795	66
	Total	205.15	236.775	88
Amylase Discharge	Death	255.77	194.499	22
	Discharge	74.32	22.230	66
	Total	119.68	125.479	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Outcome of the disease and Mean amylase level at admission, day two and at discharge:

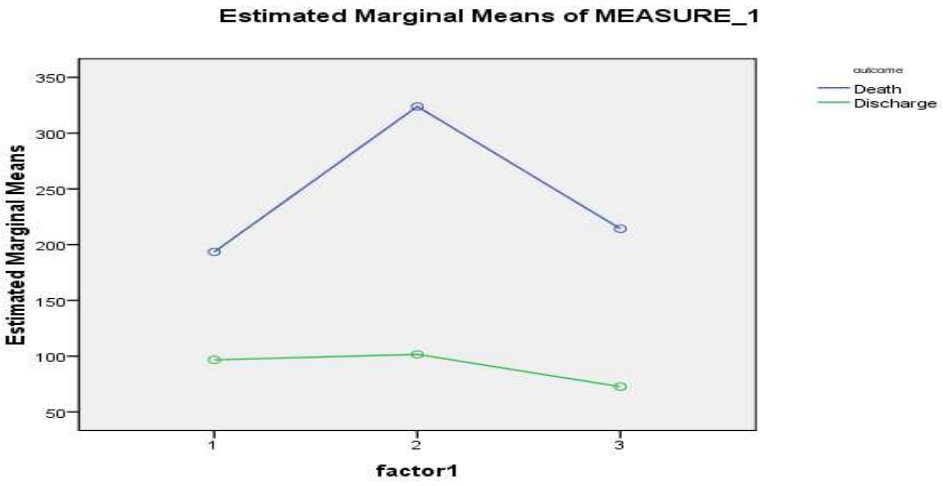


22) Outcome of the disease and mean lipase level:

	Outcome	Mean	Std. Deviation	N
Lipase Day 1	Death	193.50	92.758	22
	Discharge	96.68	70.838	66
	Total	120.89	87.199	88
Lipase Day 2	Death	323.91	239.450	22
	Discharge	101.59	109.032	66
	Total	157.17	179.152	88
Lipase Discharge	Death	214.27	171.742	22
	Discharge	72.64	18.158	66
	Total	108.05	105.691	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Outcome of the disease and Mean Lipase level at admission, day two and at discharge:

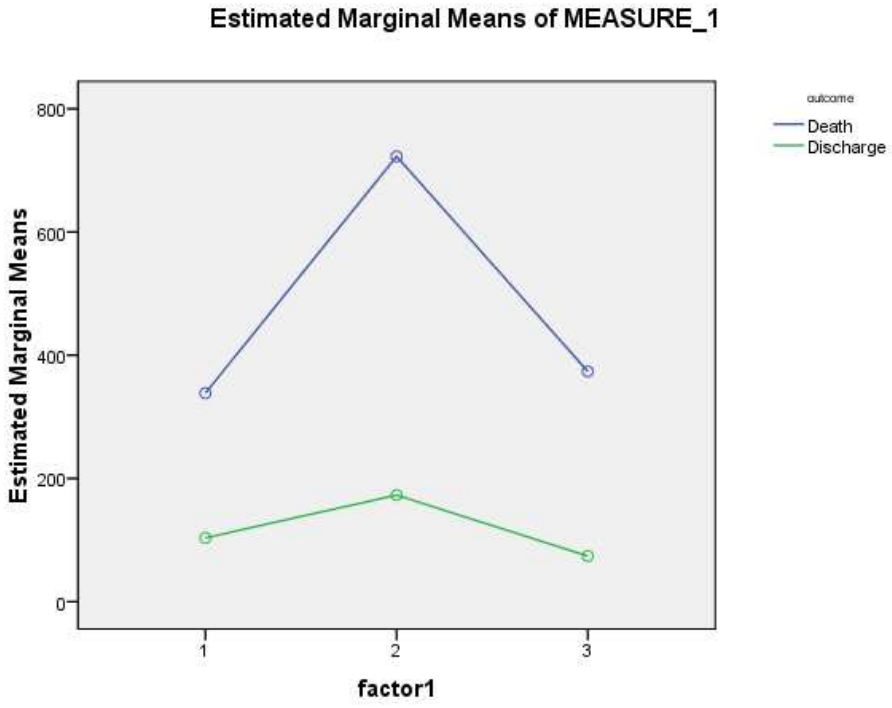


23) Outcome of the disease and Mean Creatine Kinase level:

	Outcome	Mean	Std. Deviation	N
CK Day 1	Death	338.45	210.731	22
	Discharge	103.45	101.487	66
	Total	162.20	169.965	88
CK Day 2	Death	722.68	507.800	22
	Discharge	173.06	359.454	66
	Total	310.47	464.831	88
CK Discharge	Death	373.59	365.391	22
	Discharge	73.95	26.363	66
	Total	148.86	223.100	88

p-Value<0.001 (Repeated Measures ANOVA used)

Line diagram of Outcome of the disease and Mean creatine Kinase level at admission, day two and at discharge:



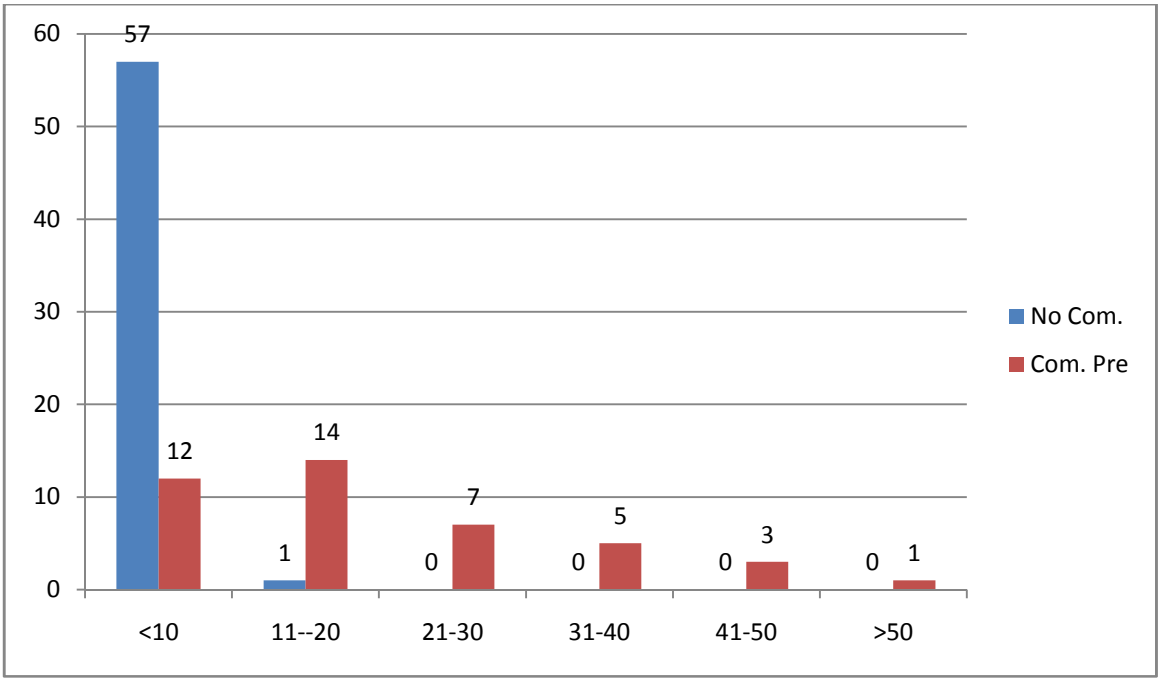
24) Cross tabulation between Atropine dose and Complications:

			Complications		Total
			No	Yes	
Atropine Dose (No.of vials)	10	Count	57	12	69
		% within atrodos	82.6%	17.4%	100.0%
	11-20	Count	1	14	15
		% within atrodos	6.7%	93.3%	100.0%
	21-30	Count	0	7	7
		% within atrodos	.0%	100.0%	100.0%
	31-40	Count	0	5	5
		% within atrodos	.0%	100.0%	100.0%
	41-50	Count	0	3	3
		% within atrodos	.0%	100.0%	100.0%
	>50	Count	0	1	1
		% within atrodos	.0%	100.0%	100.0%
Total		Count	58	42	100

			Complications		
			No	Yes	Total
Atropine Dose (No.of vials)	10	Count	57	12	69
		% within atrodos	82.6%	17.4%	100.0%
	11-20	Count	1	14	15
		% within atrodos	6.7%	93.3%	100.0%
	21-30	Count	0	7	7
		% within atrodos	.0%	100.0%	100.0%
	31-40	Count	0	5	5
		% within atrodos	.0%	100.0%	100.0%
	41-50	Count	0	3	3
		% within atrodos	.0%	100.0%	100.0%
	>50	Count	0	1	1
		% within atrodos	.0%	100.0%	100.0%
Total		Count	58	42	100
		% within atrodos	58.0%	42.0%	100.0%

Fisher's Exact Test value = 56.87 p-Value = <0.001

Bar diagram between dose of atropine and complications:

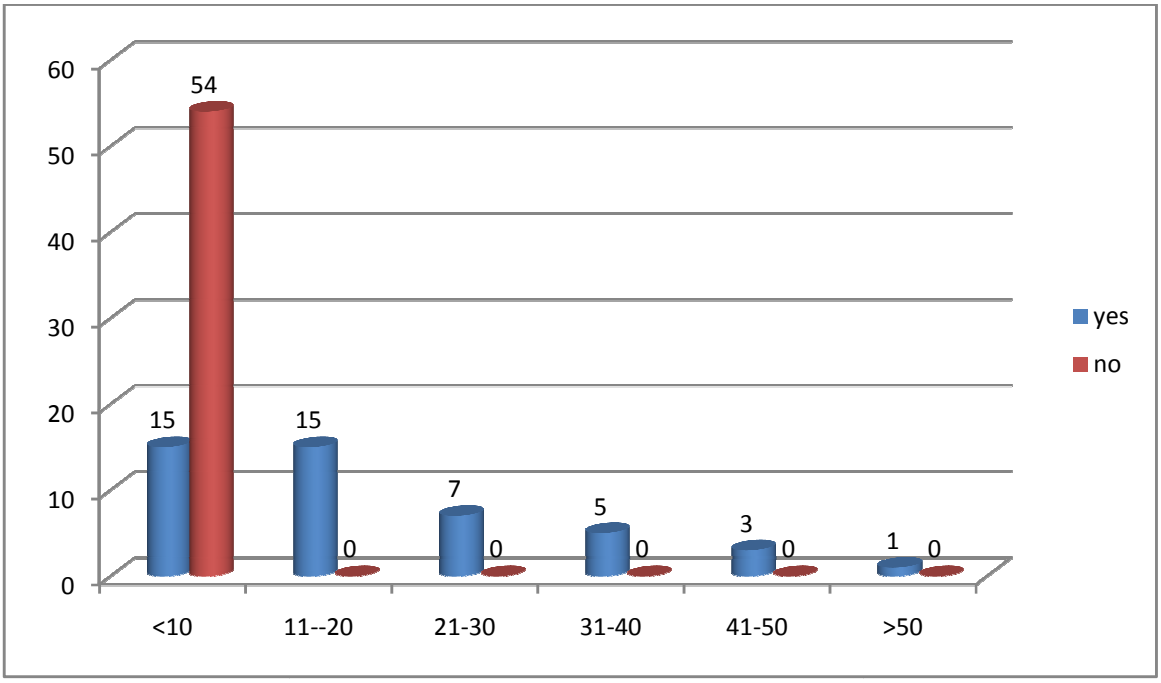


25) Cross tabulation between Atropine dose and need for ventilator:

			Ventilator		
			No	Yes	Total
Atropine Dose (No.of Vials)	10	Count	54	15	69
		% within atrodos	78.3%	21.7%	100.0%
	11-20	Count	0	15	15
		% within atrodos	.0%	100.0%	100.0%
	21-30	Count	0	7	7
		% within atrodos	.0%	100.0%	100.0%
	31-40	Count	0	5	5
		% within atrodos	.0%	100.0%	100.0%
	41-50	Count	0	3	3
		% within atrodos	.0%	100.0%	100.0%
	>50	Count	0	1	1
		% within atrodos	.0%	100.0%	100.0%
Total		Count	54	46	100
		% within atrodos	54.0%	46.0%	100.0%

Fisher's Exact Test value = 38.87 p-Value = <0.001

Bar diagram between dose of atropine and Need for Ventilator:

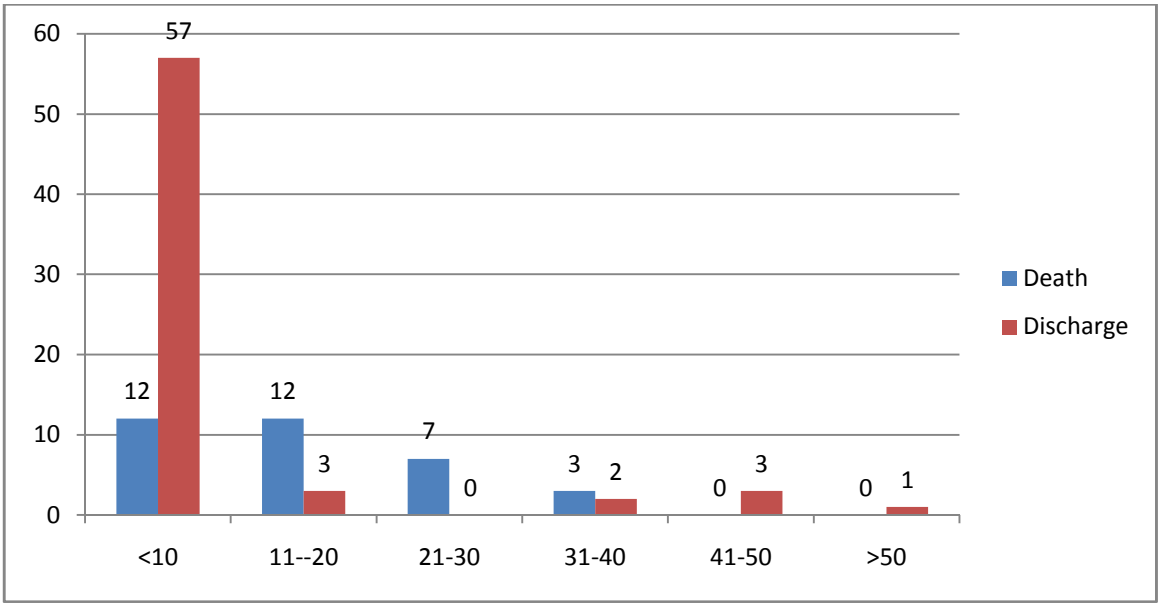


26) Cross tabulation between Atropine dose and Outcome:

			Outcome		
			Death	Discharge	Total
Atropine Dose (No. of Vials)	10	Count	12	57	69
		% within atrodos	17.4%	82.6%	100.0%
	11-20	Count	12	3	15
		% within atrodos	80.0%	20.0%	100.0%
	21-30	Count	7	0	7
		% within atrodos	100.0%	.0%	100.0%
	31-40	Count	3	2	5
		% within atrodos	60.0%	40.0%	100.0%
	41-50	Count	0	3	3
		% within atrodos	.0%	100.0%	100.0%
	>50	Count	0	1	1
		% within atrodos	.0%	100.0%	100.0%
Total		Count	34	66	100
		% within atrodos	34.0%	66.0%	100.0%

Fisher's Exact test value = 38.083 P- Value <0.001

Bar diagram between dose of atropine and Outcome:



27) Independent Samples Tests used

A) Serum levels of Ach, Amylase, Lipase and CK on day of admission and complications

	Complications	N	Mean	Std. Deviation	Std. Error Mean	Sig. (2-tailed)
Ach Day 1	Yes	42	508.26	516.020	79.624	
	No	58	4469.52	2363.870	310.391	<0.001**
Amylase Day 1	Yes	42	263.67	145.233	22.410	<0.001**
	No	58	128.33	122.920	16.140	
Lipase Day 1	Yes	42	211.79	139.029	21.453	<0.001**
	No	58	92.07	69.571	9.135	
CK Day 1	Yes	42	329.88	243.764	37.614	
	No	58	81.09	52.098	6.841	<0.001**

B) Serum levels of Ach, Amylase, Lipase and CK on day of admission and Intermediate Syndrome

	IMS	N	Mean	Std. Deviation	Std. Error Mean	Sig. (2-tailed) P-Value
Ach Day 1	Yes	21	631.43	969.604	211.585	
	No	79	3383.78	2696.610	303.392	.000
Amylase Day 1	Yes	21	222.57	134.142	29.272	
	No	79	175.23	150.859	16.973	.194
Lipase Day 1	Yes	21	175.43	98.647	21.527	
	No	79	133.56	123.714	13.919	.155
CK Day 1	Yes	21	339.57	221.049	48.237	
	No	79	144.65	178.714	20.107	.000

C) Serum levels of Ach, Amylase, Lipase and CK on day of admission and Ventilator Requirement

	Ventilator	N	Mean	Std. Deviation	Std. Error Mean	Sig. (2-tailed)
aceone	Yes	46	602.96	760.889	112.187	
	No	54	4682.28	2266.494	308.431	.<0.001
amyone	Yes	46	263.72	154.884	22.836	<0.001
	No	54	118.26	103.445	14.077	
lipaone	Yes	46	211.87	143.509	21.159	<0.001
	No	54	83.13	38.621	5.256	
ckdone	Yes	46	317.80	238.783	35.207	
	No	54	72.94	28.723	3.909	<0.001

D) Serum levels of Ach and Serum levels of Amylase, Lipase and CK on day of admission, day 2 and day of discharge

		N	Mean	Std. Deviation	95% Confidence Interval for Mean		Minimum	Maximum	Sig. (2-tailed)
					Lower Bound	Upper Bound			
Ach Levels	1	30	5163.70	2141.799	4363.94	5963.46	1586	9778	
	2	27	3990.96	2185.931	3126.24	4855.69	751	8911	.<0.001
	Disc	43	416.56	317.179	318.94	514.17	116	1894	
	Total	100	2805.79	2681.159	2273.79	3337.79	116	9778	
Amylase levels	1	30	84.73	48.225	66.73	102.74	32	195	
	2	27	154.59	131.818	102.45	206.74	35	543	.<0.001
	Disc	43	274.44	152.943	227.37	321.51	56	651	
	Total	100	185.17	148.127	155.78	214.56	32	651	
Lipase levels	1	30	71.53	17.716	64.92	78.15	39	120	
	2	27	93.78	49.825	74.07	113.49	40	217	.<0.001
	Disc	43	222.26	142.692	178.34	266.17	68	718	
	Total	100	142.35	119.659	118.61	166.09	39	718	
CK Levels	1	30	75.17	38.930	60.63	89.70	40	243	
	2	27	97.44	82.926	64.64	130.25	36	386	.<0.001
	Disc	43	317.95	246.264	242.16	393.74	72	1315	
	Total	100	185.58	203.475	145.21	225.95	36	1315	

DISCUSSION

DISCUSSION

An observational study conducted in Toxicology ward in Rajiv Gandhi Government General Hospital, Institute of Internal Medicine Madras Medical College, Chennai. The study enrolled 100 patients admitted with OPC poisoning after applying inclusion and exclusion criteria. The study period was 6 months from November 2017 to April 2018.

Out of 100 patients, the study population comprised of 25% females and 75% males. This finding is consistent with study conducted by S.Shivakumar and K.Raghavan et al of Tamilnadu who reported 165 cases of OPC poisoning with male predominance in sex distribution. KuntalBattacharya et al from Kolkata showed male predominance. A similar pattern of male dominance observed in Mangalore and Srilankacase series. In South India, as males are more involved in spraying pesticides. The mean age of study population was 38.49 years and Standard deviation of 16.17. Mean age group was 30+ 15 years in a Turkey study by Murat Sungur et al.

The predominant age group of the study population were in the age group of 21-30 years (29 cases). 91% of cases with age <30 years observed by Karalliede L., Senanayake N. et al of Srilanka. A study in Mangalore showed more in cases in 20-30 years (36.6%) This study shows that the target age group in younger age and the need for improving the management protocol and decreasing the mortality.

Majority of the patients admitted were belonging to Non- Agriculture occupation group.Non-Agriculturists were exposed more to OPC compounds with suicidal intention. The most common OP compound ingested was Monocrotophos followed by Chlorpyrifos. Kunta l bhattacharya et al described the most frequent compound as Chlorpyrifos. In our study, it was also noted that when the quantity of exposure exceeded more than 75ml it resulted in death with more than 80%.

The mortality rate in our study group is 34%. Sundaram et al study showed mortality rate of 22.5%. In our study, POP scoring was much reliable and was correlated with duration of presentation, outcome, levels of mean serum AchE, Amylase, Lipase, Creatine Kinase, duration of hospital stay, development of Intermediate Syndrome. The initial serum CK with Clinical severity by POP scoring and outcome study was correlated by Kunal Bhattacharya et al of Kolkata. Mild POP score seen in 30%, Moderate POP score in 27% and Severe POP score seen in 43%. The death rate in patients with Severe POP score was 79.1% (34 out of 43). The mean levels of Serum AchE decreased whereas the mean level of serum Amylase, Lipase and Creatine Kinase in patients having Severe POP score. Thus AchE and Amylase, Lipase and CK have negative correlation.

The initial rise in Serum CK in severe acute OPC poisoning is probably due to the presence of muscle fibre necrosis. This occurred even before the development of Intermediate syndrome in which CK level is expected to rise. Hence it can be used as predictor for IMS. With good management, CK levels

may be reduced to normal within 5 days, if patient does not develop IMS. The levels of Amylase and Lipase are increased due to increasing Cholinergic activity and the occurrence of pancreatitis caused by OPC poisoning.

In our study, raised serum Amylase, Lipase and CK levels significantly correlated with initial clinical severity by POP scoring, increasing atropine requirement, hospital stay duration, IMS, complications like arrhythmias, renal failure, pancreatitis, coma and outcome and it more significantly correlated with the initial serum levels at admission. Raised levels of Serum Amylase, Lipase and CK levels had negative correlation with the Serum AchE levels at admission.

Hence, we have concluded that levels of Serum Amylase, Lipase and CK can be used as parameters for assessing the severity and Ouctome of Acute OPC poisoning replacing Serum AchE levels. Hence, it is our opinion from the study that increased Serum level of Amylase, Lipase and CK will correlate with poor clinical outcome.

CONCLUSION

CONCLUSIONS

OPC poisoning is one of the most common cause of suicide related deaths in our country and the incidence is increasing day by day. In our study

1) Most of the patients were males (75%).
2) The mean age of the study population was 38.49 years and standard deviation of 16.17.
3) Age group between 21 to 30 yrs are more commonly encountered in poisoning.
4) There is male preponderance in our study.
5) The most common poisonous OPC consumed is Monocrotophos.
6) Quantity of the poison consumed correlate with the severity of poisoning. There was a good correlation between the severity of the POP scale and the outcome of the patient.
7) The mortality rate in our study group is 34%.
8) In our study, POP scoring was much reliable and was correlated with duration of presentation, outcome, levels of mean serum AchE, Amylase, Lipase, CK, duration of hospital stay, development of Intermediate Syndrome which were statistically significant.
9) The Serum levels of Amylase, Lipase and CK levels significantly correlated with initial clinical severity by POP scoring, increased atropine requirement, hospital stay duration , ventilator requirement and outcome

10) The Serum levels of Amylase, Lipase and CK levels significantly correlated with Intermediate Syndrome and complications and it more significantly correlated with the initial serum levels at admission.

11) Thus with morbidity and mortality, raised serum levels of Amylase, Lipase and CK levels had negative correlation with the Serum AchE levels at admission.

12) We concluded that levels of Serum Amylase, Lipase and CK can be used as parameters for assessing the severity and Ouctome of Acute OPC poisoning replacing Serum AchE levels.

13) Hence, it is our opinion from the study that increased Serum level of Amylase, Lipase and CK will correlate with poor clinical outcome and can be used as newer biochemical markers in predicting the severity of OPC poisoning.

LIMITATIONS OF THE STUDY

LIMITATIONS OF THE STUDY

1) The number of biochemical markers (Serum Amylase, Lipase and CK) for predicting the severity of OPC poisoning is more compared to the Serum Acetylcholinesterase.

2) Due to financial constraints the measurements of Serum Amylase, Lipase and CK may not be feasible in all the health care set up.

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ANNEXURES

PROFORMA

NAME :

AGE/SEX :

IP No. :

OCCUPATION :

II.POISONING

COMPOUND	
AMOUNT	
TIME AND DATE OF CONSUMPTION	

III. SYMPTOMS

VOMITING	
LOOSE STOOLS	
ABDOMINAL PAIN	
SALIVATION/ LACRIMATION/SWEATING	
DYSPNOEA	
HAEMATURIA	
BLURRING OF VISION	
SEIZURES	
LOSS OF CONSCIOUSNESS	

IV.PAST HISTORY:

DIABETES MELLITUS	
HYPERTENSION	
BRONCHIAL ASTHMA/COPD	
TUBERCULOSIS	
OTHERS	

V.PERSONAL HISTORY:

SMOKING	
ALCOHOLISM	
OTHER HABITS	

VI. VITALS :

PULSE RATE	
BLOOD PRESSURE	
RESPIRATORY RATE	
TEMPERATURE	
SPO2	

VII.SYSTEMIC EXAMINATION:

CVS	
RS	
ABDOMEN	
CNS	

VIII. INVESTIGATIONS

CBC	
LFT	
RFT	
SE	
RBS	
URINE (R/E)	
ECG	

ANNEXURE II

PERADENIYA ORGANOPHOSPHORUS SCALE

PARAMETERS	0	1	2	SCORE
PUPIL SIZE	≥2 mm	<2mm	Pinpoint	
RESPIRATORY RATE	<20/ Min	≥20/min	≥20/min with central cyanosis	
HEART RATE	>60/ Min	41-60/min	<40/min	
FASCICULATION	None	Present Generalised/ continuous	Both generalised and continuous	
LEVEL OF CONSCIOUSNESS	Conscious and rationale	Impaired response to verbal commands	No response to verbal commands	
SEIZURE	Absent	Present	-	
GRADE	Mild (0-3)	Moderate (4-7)	Severe (8-11)	

ANNEXURE III

SERIAL ESTIMATION OF SERUM ACETYLCHOLINESTERASE, AMYLASE, LIPASE AND CREATINE KINASE

	DAY 1 U/L	**DAY 2 U/L**	**ON DISCHARGEU/L**
SERUM ACETYL CHOLINESTERASE			
SERUM AMYLASE			
SERUM LIPASE			
SERUM CREATINE KINASE			
CLINICAL SCORING			
ATROPINE REQUIREMENT			
COMPLICATIONS IF ANY			
DURATION OF THE HOSPITAL			

ETHICAL COMMITTEE APPROVAL

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To

Dr.M.Shivanathan
PG in MD General Medicine
Institute of Internal Medicine
Madras Medical College
Chennai 600 003

Dear Dr.M.Shivanathan,

The Institutional Ethics Committee has considered your request and approved your study titled **"CORRELATION OF SERUM AMYLASE, LIPASE AND CREATINE KINASE IN PREDICTING THE SEVERITY OF ORGANOPHOSPHORUS POISONING " - NO.05052017**

The following members of Ethics Committee were present in the meeting hold on **02.05.2017** conducted at Madras Medical College, Chennai 3

1.Prof.Dr.C.Rajendran, MD.,	:Chairperson
2.Prof.R.Narayana Babu, MD.,DCH.,Dean, MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	:Member Secretary
4.Prof.S.Suresh,MS.,Prof.of Surgery,MMC, Ch-3	: Member
5.Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3	: Member
6.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
7.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
8.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

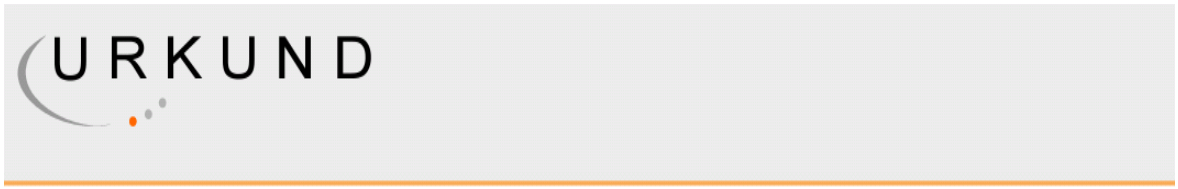
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

PLAGIARISM SCREENSHOT



Urkund Analysis Result

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Instances where selected sources appear:

9

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"CORRELATION OF SERUM AMYLASE, LIPASE AND CREATINE KINASE IN PREDICTING THE SEVERITY OF ORGANOPHOSPHORUS POISONING"** of the candidate **Dr.M.SHIVANATHAN** with registration Number for the award of **M.D** in the branch of **GENERAL MEDICINE.** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **4** percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

INFORMATION SHEET

We are conducting a study on **"CORRELATION OF SERUM AMYLASE, LIPASE AND CREATINE KINASE IN PREDICTING THE SEVERITY OF ORGANOPHOSPHORUS POISONING"** among patients admitted in Toxicology ward with Organophosphorus poisoning in Rajiv Gandhi Government General Hospital, Chennai and for that your blood sample may be valuable to us. The purpose of this study is to correlate the levels of Serum Amylase, Lipase and Creatine Kinase with Serum Acetylcholinesterase in assessing the severity of Organophosphorus poisoning.

We are selecting certain cases and if you are found eligible, we may perform extra tests and special studies which in any way do not affect your final report or management. The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled. The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator — Signature of Participant

Date : — Place :

PATIENT CONSENT FORM

Study Detail	:	**CORRELATION OF SERUM AMYLASE, LIPASE AND CREATINE KINASE IN PREDICTING THE SEVERITY OF ORGANOPHOSPHORUS POISONING**
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name	:	
Patient's Age	:	
Identification Number	:	

Patient may check (☑) these boxes

I confirm that I have understood the purpose of the study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it,even if I withdraw ☐

from the study I agree to this access. ☐

However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression

Patient's Name and Address

Signature of Investigator

S.No	Age	Agecate	Sex	Occupation	Compound	Quantity	Outcmum	Quantcate	Duration	Popscore	aceone	acetwo	acedis	amyone	amytwo	amdis	lipaone	lipatwo	lipadis	ckdone	ckdtwo	ckddis	intermediatesyn	atropinedose	Ventilator	v17	Complications	hospstay	outcome	durcat	atrodoscat	outcat	popscorenum
1	45	41-50	M	Agri	Phorate	30	2	26-50	4	Moderate	843	950	4,065	178	152	40	180	126	66	140	128	46	No	6	No	-	No	7	Discharge	4-6	10	1	2
2	25	21-30	F	Non-Agri	Monocrotphos	150	1	>100	16	Severe	158	-	-	640	-	-	718	-	-	1,315	-	-	No	20	Yes	1	Yes	1	Death	>12	11-20	0	3
3	48	41-50	M	Agri	Malathion	15	2	<25	3	Mild	4,536	5,420	6,228	36	37	38	120	110	106	139	130	133	No	3	No	-	No	3	Discharge	<3	10	1	1
4	35	31-40	M	Non-Agri	Temephos	20	2	<25	4	Mild	5,684	6,632	6,637	48	46	50	67	58	62	56	52	44	No	2	No	-	No	2	Discharge	4-6	10	1	1
5	21	21-30	F	Non-Agri	Profenofos	100	1	76-100	8	Severe	224	180	2,335	580	1,056	298	436	884	188	142	438	150	Yes	32	Yes	9	Yes	15	Death	7-9	31-40	0	3
6	28	21-30	M	Non-Agri	Monocrotphos	100	1	76-100	7	Severe	368	254	3,454	120	223	95	69	80	60	128	296	146	Yes	24	Yes	3	Yes	7	Death	7-9	21-30	0	3
7	48	41-50	M	Agri	Primiphos	50	2	26-50	2	Moderate	2,987	3,336	4,853	68	65	65	53	58	52	46	40	42	No	4	No	-	No	2	Discharge	<3	10	1	2
8	70	>60	M	Agri	Chlorpyrifos	150	1	>100	6	Severe	358	-	-	564	-	-	667	-	-	530	-	-	No	16	Yes	1	Yes	1	Death	4-6	11-20	0	3
9	21	21-30	F	Non-Agri	Endosulphan	25	2	<25	2	Mild	3,647	4,688	5,536	104	78	52	67	86	48	56	50	40	No	3	No	-	No	3	Discharge	<3	10	1	1
10	38	31-40	F	Non-Agri	Dimethoate	30	2	26-50	3	Mild	5,985	3,882	5,232	64	72	62	56	63	51	48	61	45	No	3	No	-	No	4	Discharge	<3	10	1	1
11	38	31-40	M	Non-Agri	Triazophos	25	2	<25	2	Moderate	4,165	3,662	6,345	50	54	46	43	45	42	36	38	35	No	5	No	-	No	6	Discharge	<3	10	1	2
12	50	41-50	M	Agri	Diazinon	100	1	76-100	6	Severe	287	195	366	289	395	672	263	492	621	448	735	1,254	Yes	18	Yes	2	Yes	5	Death	4-6	11-20	0	3
13	41	41-50	M	Non-Agri	Quinalphos	25	2	<25	3	Mild	3,835	4,235	7,647	63	68	58	64	79	62	48	55	46	No	3	No	-	No	3	Discharge	<3	10	1	1
14	29	21-30	F	Non-Agri	Chlorpyrifos	15	2	<25	1	Mild	5,432	5,910	6,341	42	38	41	47	43	40	50	52	48	No	3	No	-	No	3	Discharge	<3	10	1	1
15	20	<20	M	Non-Agri	Monocrotphos	150	1	>100	5	Severe	389	165	1,563	128	431	496	186	385	421	266	761	235	Yes	26	Yes	2	Yes	6	Death	4-6	21-30	0	3
16	60	51-60	F	Agri	Dicrotophos	75	2	51-75	8	Moderate	2,180	1,672	5,839	51	42	44	64	75	60	338	983	138	Yes	52	Yes	14	Yes	20	Discharge	7-9	>50	1	2
17	37	31-40	F	Non-Agri	Monocrotphos	100	1	76-100	3	Severe	1,894	759	580	573	861	539	238	654	358	490	875	1,236	No	25	Yes	3	Yes	3	Death	<3	21-30	0	3
18	34	31-40	F	Non-Agri	Diazinon	50	2	26-50	5	Moderate	4,376	3,852	6,479	35	40	42	52	58	46	386	971	136	Yes	14	Yes	4	No	8	Discharge	4-6	11-20	1	2
19	33	31-40	F	Non-Agri	Monocrotphos	15	2	<25	3	Mild	3,395	4,521	7,832	32	45	48	68	61	70	116	120	64	No	6	No	-	No	4	Discharge	<3	10	1	1
20	35	31-40	M	Agri	Diazinon	25	2	<25	2	Mild	4,751	3,674	6,790	48	52	40	57	51	50	109	123	96	No	2	No	-	No	3	Discharge	<3	10	1	1
21	18	<20	M	Non-Agri	Ethion	30	2	26-50	2	Moderate	4,569	3,357	4,798	199	264	96	172	160	125	74	78	69	No	4	No	-	No	3	Discharge	<3	10	1	2
22	60	51-60	M	Agri	Quinalphos	50	2	26-50	5	Moderate	2,705	942	4,521	176	210	98	180	174	97	68	62	60	No	6	No	-	No	5	Discharge	4-6	10	1	2
23	58	51-60	M	Non-Agri	Phosphomidon	75	1	51-75	4	Severe	586	295	2,628	356	1,328	256	290	972	275	199	568	196	Yes	10	Yes	2	Yes	6	Death	4-6	10	0	3
24	22	21-30	F	Non-Agri	Phosphomidon	100	2	76-100	3	Severe	369	158	4,984	293	951	110	264	862	95	688	2,568	125	Yes	42	Yes	18	Yes	26	Discharge	<3	41-50	1	3
25	70	>60	F	Agri	Fenthion	25	2	<25	2	Mild	1,586	995	2,864	190	158	96	68	66	60	108	78	76	No	12	Yes	2	Yes	2	Discharge	<3	11-20	1	1
26	30	21-30	M	Non-Agri	Dimethoate	75	2	51-75	5	Severe	964	391	4,835	175	531	65	183	156	110	328	688	140	Yes	34	Yes	9	Yes	14	Discharge	4-6	31-40	1	3
27	14	<20	M	Non-Agri	Phorate	50	2	26-50	4	Moderate	751	258	3,513	68	75	66	57	75	68	73	80	71	No	4	No	-	No	5	Discharge	4-6	10	1	2
28	50	41-50	M	Agri	Monocrotphos	150	1	>100	10	Severe	239	176	898	130	115	106	75	84	78	195	291	358	No	25	Yes	3	Yes	3	Death	10-12	21-30	0	3
29	38	31-40	M	Non-Agri	Dichlorphos	30	2	26-50	2	Mild	3,584	3,395	4,216	74	85	71	78	70	75	68	59	65	No	4	No	-	No	3	Discharge	<3	10	1	1
30	17	<20	M	Non-Agri	Malathion	25	2	<25	3	Mild	2,230	1,675	4,105	190	110	108	98	134	90	243	185	147	No	12	Yes	2	Yes	5	Discharge	<3	11-20	1	1
31	30	21-30	M	Non-Agri	Monocrotphos	150	1	>100	4	Severe	364	-	-	356	-	-	285	-	-	451	-	-	No	20	Yes	1	Yes	1	Death	4-6	11-20	0	3

32	42	41-50	M	Agri	Ethion	30	2	26-50	3	Moderate	4,130	3,358	5,891	295	335	95	86	95	80	75	72	74	No	6	No	-	No	4	Discharge	<3	10	1	2
33	22	21-30	M	Non-Agri	Triazophos	25	2	<25	2	Mild	3,156	4,239	5,510	128	106	93	78	74	70	65	68	62	No	3	No	-	No	3	Discharge	<3	10	1	1
34	20	<20	F	Non-Agri	Chlorpyrifos	100	1	76-100	22	Severe	566	391	1,753	358	893	751	295	330	680	595	1,682	1,250	No	22	Yes	4	Yes	4	Death	>12	21-30	0	3
35	38	31-40	M	Non-Agri	Chlorpyrifos	30	2	26-50	3	Moderate	3,985	2,951	4,139	65	69	66	50	54	52	62	89	68	No	6	No	-	No	4	Discharge	<3	10	1	2
36	26	21-30	F	Non-Agri	Phorate	100	1	76-100	5	Severe	687	416	1,853	110	431	329	98	446	320	683	1,981	525	Yes	20	Yes	3	Yes	7	Death	4-6	11-20	0	3
37	28	21-30	F	Non-Agri	Bromophos	25	2	<25	2	Mild	4,530	3,769	4,612	65	58	62	72	68	70	66	64	65	No	3	No	-	No	3	Discharge	<3	10	1	1
38	16	<20	F	Non-Agri	Chlorpyrifos	100	2	76-100	8	Severe	534	320	2,560	56	54	52	68	64	66	72	70	68	No	38	Yes	12	Yes	14	Discharge	7-9	31-40	1	3
39	32	31-40	M	Non-Agri	Fenthion	30	2	26-50	4	Moderate	3,568	2,971	4,185	543	287	106	217	174	103	95	88	92	No	7	No	-	No	5	Discharge	4-6	10	1	2
40	22	21-30	M	Non-Agri	Malathion	20	2	<25	3	Mild	4,509	3,784	4,261	46	51	48	55	59	56	86	90	85	No	2	No	-	No	3	Discharge	<3	10	1	1
41	46	41-50	F	Agri	Dicrotophos	35	2	26-50	2	Moderate	2,981	3,655	5,894	231	179	98	95	120	84	49	95	70	No	5	No	-	No	4	Discharge	<3	10	1	2
42	41	41-50	M	Non-Agri	Monocrotphos	65	2	51-75	6	Severe	795	431	2,859	651	438	118	519	295	95	98	89	85	No	6	Yes	2	No	4	Discharge	4-6	10	1	3
43	43	41-50	M	Non-Agri	Profenofos	50	2	26-50	5	Severe	1,102	358	2,781	176	256	105	95	88	76	80	66	75	No	10	Yes	3	No	5	Discharge	4-6	10	1	3
44	30	21-30	M	Agri	Phorate	75	2	51-75	2	Moderate	3,265	2,630	4,031	543	210	90	86	71	78	89	80	84	No	9	No	-	No	5	Discharge	<3	10	1	2
45	24	21-30	F	Non-Agri	Chlorpyrifos	10	2	<25	3	Mild	3,150	4,162	4,529	79	85	80	64	60	62	58	64	60	No	5	No	-	No	3	Discharge	<3	10	1	1
46	50	41-50	M	Non-Agri	Malathion	15	2	<25	1	Mild	3,995	4,951	5,368	68	74	70	61	58	64	52	59	56	No	2	No	-	No	3	Discharge	<3	10	1	1
47	33	31-40	F	Non-Agri	Chlorpyrifos	35	2	26-50	3	Moderate	3,570	2,932	4,960	210	162	94	98	87	91	73	99	67	No	7	No	-	No	5	Discharge	<3	10	1	2
48	40	31-40	F	Non-Agri	Primiphos	20	2	<25	2	Mild	3,868	4,761	5,695	71	63	68	75	70	73	68	62	66	No	6	No	-	No	3	Discharge	<3	10	1	1
49	27	21-30	M	Non-Agri	Diazinon	25	2	<25	2	Moderate	3,164	3,908	4,521	41	45	40	42	51	48	46	52	48	No	2	No	-	No	3	Discharge	<3	10	1	2
50	26	21-30	M	Non-Agri	Quinalphos	50	2	26-50	3	Moderate	2,785	3,641	4,860	206	169	110	186	139	96	99	85	71	No	4	No	-	No	4	Discharge	<3	10	1	2
51	65	>60	M	Agri	Profenofos	20	2	<25	3	Mild	3,890	4,695	5,124	98	79	68	64	70	66	59	63	61	No	2	No	-	No	3	Discharge	<3	10	1	1
52	55	51-60	M	Non-Agri	Profenofos	100	1	76-100	5	Severe	538	-	-	310	-	-	298	-	-	238	-	-	No	18	Yes	1	Yes	1	Death	4-6	11-20	0	3
53	58	51-60	M	Agri	Fonofos	150	2	>100	5	Severe	277	331	-	420	365	-	265	210	-	198	375	-	No	6	Yes	2	Yes	2	Death	4-6	10	0	3
54	20	<20	M	Non-Agri	Monocrotphos	50	2	26-50	6	Severe	176	289	4,160	196	215	96	201	366	85	110	368	90	Yes	44	Yes	15	Yes	21	Discharge	4-6	41-50	1	3
55	50	41-50	M	Non-Agri	Chlorpyrifos	35	2	26-50	9	Moderate	1,468	2,369	4,065	98	85	82	78	84	80	75	66	70	No	2	No	-	No	5	Discharge	7-9	10	1	2
56	50	41-50	M	Agri	Chlorpyrifos	75	1	51-75	10	Severe	342	364	1,859	205	389	366	200	342	239	260	415	198	No	20	Yes	4	Yes	4	Death	10-12	11-20	0	3
57	53	51-60	M	Non-Agri	Parathion	100	1	76-100	9	Severe	132	398	1,230	199	267	220	164	256	216	316	298	206	No	8	Yes	4	Yes	4	Death	7-9	10	0	3
58	50	41-50	M	Non-Agri	Phorate	75	1	51-75	18	Severe	289	456	-	132	106	-	94	102	-	85	99	-	No	9	Yes	2	Yes	2	Death	>12	10	0	3
59	26	21-30	F	Agri	Quinalphos	30	2	26-50	3	Mild	5,608	3,659	4,102	109	98	68	96	85	70	58	66	60	No	3	No	2	No	5	Discharge	<3	10	1	1
60	32	31-40	M	Non-Agri	Monocrotphos	150	1	>100	22	Severe	344	286	-	198	275	-	210	342	-	98	199	-	No	8	Yes	-	Yes	2	Death	>12	10	0	3
61	32	31-40	M	Agri	Bromophos	25	2	<25	1	Mild	4,587	3,190	4,235	194	296	86	99	120	69	78	92	75	No	4	No	-	No	5	Discharge	<3	10	1	1
62	50	41-50	M	Agri	Chlorpyrifos	50	2	26-50	6	Moderate	3,258	2,145	4,066	140	86	90	82	71	77	195	296	138	No	9	No	-	No	6	Discharge	4-6	10	1	2
63	47	41-50	M	Non-Agri	Quinalphos	35	2	26-50	4	Moderate	6,488	3,651	5,531	210	165	88	85	78	80	56	68	62	No	4	No	-	No	5	Discharge	4-6	10	1	2
64	23	21-30	M	Non-Agri	Monocrotphos	25	2	<25	2	Mild	5,633	3,263	4,085	68	58	62	96	85	80	64	69	62	No	4	No	-	No	5	Discharge	<3	10	1	1
65	25	21-30	F	Agri	Dicrotophos	100	1	76-100	11	Severe	342	233	1,864	320	455	211	241	185	129	168	455	237	Yes	10	Yes	2	Yes	5	Death	10-12	10	0	3
66	35	31-40	F	Non-Agri	Femaphos	25	2	<25	2	Mild	8,422	3,951	5,374	66	72	68	57	61	59	55	48	52	No	3	No	-	No	4	Discharge	<3	10	1	1

67	40	31-40	M	Agri	Phoxim	20	2	<25	3	Mild	6,420	3,856	4,329	58	62	60	66	58	62	52	59	55	No	2	No	-	No	3	Discharge	<3	10	1	1
68	32	31-40	M	Non-Agri	Phosphomidon	100	1	76-100	14	Severe	145	325	1,984	189	320	166	94	210	96	236	528	201	Yes	32	Yes	11	Yes	11	Death	>12	31-40	0	3
69	85	>60	M	Agri	Chlormephos	150	1	>100	19	Severe	320	186	1,630	168	145	96	88	120	95	148	369	381	Yes	18	Yes	2	Yes	5	Death	>12	11-20	0	3
70	45	41-50	M	Non-Agri	Bromophos	25	2	<25	3	Mild	8,861	3,084	4,232	88	79	75	68	74	72	67	75	71	No	2	No	-	No	5	Discharge	<3	10	1	1
71	39	31-40	M	Agri	Monocrotphos	75	1	51-75	4	Severe	211	-	-	268	-	-	199	-	-	295	-	-	No	10	Yes	1	Yes	1	Death	4-6	10	0	3
72	18	<20	F	Non-Agri	Profenofos	35	2	26-50	8	Moderate	8,755	3,920	5,108	165	108	94	89	75	80	76	84	80	No	4	No	-	No	5	Discharge	7-9	10	1	2
73	18	<20	F	Non-Agri	Phorate	25	2	<25	6	Moderate	8,911	3,652	5,312	98	78	86	72	65	70	66	62	64	No	3	No	-	No	5	Discharge	4-6	10	1	2
74	67	>60	M	Non-Agri	Phosphomidon	100	1	76-100	18	Severe	322	-	-	236	-	-	168	-	-	295	-	-	No	10	Yes	1	Yes	1	Death	>12	10	0	3
75	27	21-30	M	Non-Agri	Phoxim	25	2	<25	5	Mild	8,508	3,755	4,320	65	60	62	58	68	64	72	58	65	No	2	No	-	No	3	Discharge	4-6	10	1	1
76	78	>60	M	Agri	Monocrotphos	75	1	51-75	14	Severe	266	385	1,620	218	320	158	184	142	140	786	595	243	Yes	12	Yes	1	Yes	5	Death	>12	11-20	0	3
77	73	>60	M	Agri	Quinalphos	35	2	26-50	8	Moderate	8,866	3,964	5,320	78	69	75	79	73	76	83	79	81	No	4	No	-	No	6	Discharge	7-9	10	1	2
78	52	51-60	M	Non-Agri	Chlorpyrifos	35	2	26-50	4	Moderate	3,644	2,769	4,062	90	84	88	79	72	76	65	69	63	No	6	No	-	No	6	Discharge	4-6	10	1	2
79	55	51-60	M	Agri	Monocrotphos	150	1	>100	14	Severe	167	325	1,968	108	199	145	98	186	154	154	596	235	Yes	12	Yes	5	Yes	5	Death	>12	11-20	0	3
80	20	<20	M	Non-Agri	Phosphomidon	100	1	76-100	8	Severe	422	-	-	360	-	-	225	-	-	256	-	-	No	10	Yes	1	Yes	1	Death	7-9	10	0	3
81	42	41-50	M	Agri	Dicrotophos	75	2	51-75	18	Severe	116	875	3,289	195	125	106	185	130	98	200	437	98	Yes	8	Yes	2	No	6	Discharge	>12	10	1	3
82	45	41-50	M	Agri	Femaphos	35	2	26-50	4	Mild	8,544	3,162	4,158	85	92	82	83	78	79	62	76	70	No	2	No	-	No	3	Discharge	4-6	10	1	1
83	65	>60	M	Non-Agri	Dicrotophos	35	2	26-50	9	Moderate	6,554	3,262	4,086	118	92	99	130	102	89	85	92	88	No	4	No	-	No	5	Discharge	7-9	10	1	2
84	25	21-30	M	Non-Agri	Quinalphos	25	2	<25	4	Mild	9,778	3,968	5,264	68	59	62	66	58	60	76	68	74	No	2	No	-	No	3	Discharge	4-6	10	1	1
85	75	>60	M	Non-Agri	Phoxim	35	2	26-50	6	Mild	8,766	3,155	4,853	195	135	89	96	85	92	84	80	82	No	4	No	-	No	5	Discharge	4-6	10	1	1
86	22	21-30	M	Non-Agri	Monocrotphos	150	1	>100	16	Severe	213	389	1,235	295	195	123	251	184	110	368	451	230	No	8	Yes	3	Yes	3	Death	>12	10	0	3
87	50	41-50	M	Non-Agri	Chlorpyrifos	150	2	>100	6	Severe	548	1,535	3,455	136	104	85	93	88	90	128	95	86	No	6	No	-	No	5	Discharge	4-6	10	1	3
88	41	41-50	M	Agri	Monocrotphos	35	2	26-50	3	Moderate	2,375	2,589	4,532	70	66	68	65	63	60	59	63	69	No	4	No	-	No	4	Discharge	<3	10	1	2
89	43	41-50	M	Agri	Endosulphan	125	1	>100	4	Severe	254	342	217	185	237	142	210	186	80	187	586	161	No	12	Yes	5	Yes	5	Death	4-6	11-20	0	3
90	25	21-30	M	Non-Agri	Parathion	80	2	76-100	3	Severe	185	1,490	2,788	126	119	97	95	136	99	238	791	102	Yes	42	Yes	10	Yes	15	Discharge	<3	41-50	1	3
91	30	21-30	M	Non-Agri	Monocrotphos	50	1	26-50	8	Severe	190	455	585	436	386	146	296	220	128	465	1,568	195	Yes	36	Yes	11	Yes	11	Death	7-9	31-40	0	3
92	21	21-30	M	Non-Agri	Monocrotphos	80	1	76-100	6	Severe	245	546	568	373	180	105	98	210	101	782	1,636	238	Yes	28	Yes	4	Yes	7	Death	4-6	21-30	0	3
93	18	<20	M	Non-Agri	Chlorpyrifos	15	2	<25	16	Mild	3,455	3,861	5,180	32	30	28	39	35	38	40	42	48	No	2	No	-	No	3	Discharge	>12	10	1	1
94	75	>60	M	Agri	Demeton	150	1	>100	8	Severe	398	458	-	190	236	-	320	198	-	185	237	-	No	10	Yes	2	Yes	2	Death	7-9	10	0	3
95	30	21-30	M	Non-Agri	Monocrotphos	100	1	76-100	4	Severe	558	446	358	165	290	104	184	272	130	192	439	171	No	16	Yes	5	Yes	7	Death	4-6	11-20	0	3
96	27	21-30	M	Non-Agri	Malathion	50	2	26-50	14	Moderate	3,557	4,557	5,444	38	68	45	40	51	48	36	42	38	No	3	No	-	No	5	Discharge	>12	10	1	2
97	35	31-40	M	Non-Agri	Isofluorphat	80	1	76-100	7	Severe	678	556	546	208	368	103	199	286	95	238	336	173	Yes	28	Yes	5	Yes	9	Death	7-9	21-30	0	3
98	24	21-30	F	Non-Agri	Bromophos	60	2	51-75	10	Mild	4,566	3,751	4,102	68	82	74	63	71	69	52	61	57	No	9	No	-	No	4	Discharge	10-12	10	1	1
99	37	31-40	M	Non-Agri	Diazinon	30	2	26-50	8	Moderate	3,856	2,964	4,093	110	89	91	72	66	67	86	60	58	No	8	No	-	No	5	Discharge	7-9	10	1	2
100	30	21-30	M	Non-Agri	Endosulphan	150	1	>100	12	Severe	350	-	-	410	-	-	148	-	-	338	-	-	No	10	Yes	1	Yes	1	Death	10-12	10	0	3